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A CLINICAL STUDY OF THE THERAPEUTIC VALUE OF THE CALCIUM SALTS IN GASTRIC TETANY, WITH AN ANATOMICAL REPORT ON THE PARATHYROID BODIES.[1]

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Recent researches tend to show that there is an intimate relation between the various forms of tetany and an insufficiency of the parathyroid glands; they also strongly suggest that there is an equally direct and intimate relation between disturbances of the calcium contents of the tissues of the body and tetany; and, finally, that the secretion of the parathyroid bodies exerts in an as yet imperfectly understood way a controlling influence upon calcium metabolism. Numerous researches have shown the moderating effect of the calcium salts upon the hyperexcitability of the central nervous system, and the recent noteworthy study by MacCallum and Voegtlin[2] has demonstrated the controlling influence of these salts upon the spasm of experimental tetany. The results observed by them have suggested the probable therapeutic value of the calcium salts in the various forms of human tetany.

Recently an opportunity has been afforded in the Presbyterian Hospital for a study of the effect of the calcium salts in a case of

[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 11 and 12, 1909.

[2] On the Relation of Tetany to the Parathyroid Glands and to Calcium Metabolism, Jour. Exp. Med., 1909, xi, 118.

gastric tetany, and of the parathyroid bodies after death. The case is of much interest in view of the rarity of that form of gastric tetany associated with dilatation of the stomach and stagnation of its contents, of which it is an example; in the severity of the tetanic symptoms; in the prompt inhibitory effect upon the spasms of the calcium salts artificially introduced directly into the blood stream; and, finally, in the findings at autopsy.

A male, aged thirty-three years, was received in my wards in the Presbyterian Hospital on October 25, with the diagnosis of gastric tetany by my interne Doctor Vaughan, a diagnosis fully confirmed on examination of the patient. The family and personal histories, briefly, are as follows: Both parents died of pulmonary tuberculosis. The patient at times has been a heavy drinker, and especially has been a large consumer of beer. There is a history of gastric symptoms from early in 1905, at which time he was admitted to Bellevue Hospital suffering apparently from an acute gastritis of alcoholic origin; he was discharged relieved of his symptoms. A year later he was again admitted on account of a severe gastric hemorrhage following a drinking bout. A diagnosis of duodenal ulcer was made. On discharge from the hospital, and up to the date of the illness for which he was admitted to the Presbyterian Hospital, he suffered from much epigastric distress, flatulence, and frequent vomiting. He states that occasionally as much as "a gallon of green fluid" was vomited, but at no time any blood. The night before admission to my wards the patient states that he drank copiously of aërated water, nothing alcoholic. He went to bed feeling well, slept, but awoke several hours later with severe cramps in the legs and arms. He was unable to move them, but felt no pain beyond a drawn and tense feeling in the cramped muscles. He called for assistance with difficulty, as his tongue and jaws were stiff. His abdomen was distended, and he vomited several times. He sweated profusely. He was very restless. Later his affected muscles became tender and were painful. The cramps and stiffness in no way relaxed up to the time of admission.

Examination on Admission. Patient is poorly nourished; looks ill. Is unable to speak intelligibly. Is extremely restless. Temperature (rectal), 101°. Pulse, 100 and of poor quality, regular in rhythm. Blood pressure, systolic, 112 mm. Respirations, 80. The attention is at once attracted to the abdomen and to the presence of tetanic symptoms. The contour of a dilated and distended stomach is easily appreciable. The lower outline reaches a point 10 cm. below the umbilicus in the median line, and to the right the distention reaches well beyond the parasternal line. Succussion sounds can be produced readily over the whole of the distended area. Both legs are held straight and stiff, the feet in extreme extension, the toes in plantar flexion. The muscles of the calf of legs are hard, tense, and drawn. The spasm is continuous, but pressure on the nerve

trunks and bloodvessels increases, if possible, the severity of the spasm (Trousseau's sign), and the same phenomenon obtains on tapping over the motor nerves supplying the affected muscles (Chvostek's sign). The forearms are flexed at a right angle on the arms, the wrists flexed to an extreme degree and cannot be extended, the fingers flexed at right angles at the metacarpophalangeal articulations and held rigidly straight in adduction, the thumb tightly against index finger—not drawn into palm. The spasms are continuous, but, as in the case of the lower extremities, they can be increased both by Trousseau's and Chvostek's methods. The tendon reflexes appear to be about normal in both upper and lower extremities. There are continuous twitchings of the muscles of the face, which are increased by tapping over the course of the motor trunks. A slight degree of trismus is present. The musculature of the trunk is free from spasm, and it cannot be excited by mechanical irritation of the motor nerves or the muscles. The tachypnœa is striking, the respirations, as previously stated, being 80.

The stomach was at once washed out and a large quantity of greenish ill-smelling fluid was recovered. A few hours subsequent to the lavage the spasms of the upper extremities were entirely relieved, but there was no intermission in those of the lower.

October 26. The spasms of the upper extremities are again present and are continuous, and there has been no intermission in those of the lower extremities. In spite of lavage twice used in the past twenty-four hours the patient has vomited several times, 80 ounces in all; the vomited matter a greenish fluid. The patient has not voided urine since admission, and catheterization recovered only 6 ounces of urine, of specific gravity 1016, containing a trace of albumin, no glucose, a trace of indican, and a few hyaline and granular casts. Subcutaneous clyses, 1000 c.c. of a normal salt solution, were ordered to relieve, if possible, the evident dehydration of the body tissues. The temperature fell gradually during the day to 97.5° at midnight; the respirations to 20 to 24. Blood examination: Red cells, 4,910,000; white cells, 13,500; hemoglobin, 75 per cent.; color index, 0.7; polymorphonuclears, 89 per cent.; large and small lymphocytes, 9.3 per cent; transitionals, 1.7 per cent.

October 27. There has been no appreciable diminution in the spasms of the extremities, which are still continuous. In addition to lavage and subcutaneous clyses, one-half grain of a parathyroid extract, furnished by Dr. Beebe, was directed to be given three times daily by the mouth, and caffeine as a heart stimulant. The temperature has been subnormal throughout the day. In view of the pulmonary signs present, von Pirquet's tuberculin test was tried, with negative results.

October 28 (A.M.). The patient was extremely restless and irrational in the early part of the night, but after lavage and a subcutaneous clysis of 2000 c.c. of salt solution, slept quietly, with a partial

relief of the spasms of the upper extremities, but with continued extensor spasm of the muscles of the legs. During the day the spasms in the upper extremities have again been present, and there has been no intermission in those of the lower extremities. Patient very restless and irrational. In addition to the parathyroid extract, 2 grams of calcium lactate in 1200 c.c. of normal salt solution was directed to be given intravenously. The immediate effect was to quiet the great restlessness of the patient, and a few hours later there was a marked diminution in the degree of spasm in the upper extremities, and for the first time since admission, in the lower extremities. The temperature rose slightly to 100° before the use of the calcium salt, and did not rise above this after its administration. Pulse, 80 to 96; respirations, 20 to 24.

October 29 (A.M.). The patient slept quietly the greater portion of the night. There is no spasm of the upper extremities and only slight spasm (extensor) of the legs. The electrical reactions were tested for the first time and were not found to be increased. (P.M.) Four grams of calcium lactate in 1300 c.c. of normal salt solution was given intravenously. The patient fell asleep during its administration, and for the first time since admission he became entirely relaxed. Temperature, 99.5° to 100.5°; respirations, 20.

October 30. The patient slept quietly during the night. The upper extremities are free from spasm. Late in the day slight spasm of the extensor muscles of the legs was noted. Tapping over the branches of the facial nerve still elicits slight spasm in the muscles of its distribution. This can be produced only after several moments of mechanical irritation, in marked contrast to the almost instantaneous response obtained before the first administration of the calcium salt. Four grams of calcium lactate in 1000 c.c. of normal salt solution was again given intravenously in the late afternoon. Temperature, normal. Pulse, 80 to 84; respirations, 20.

October 31. The patient slept quietly with an entire absence of spasm. Both upper and lower extremities are free from spasm, but there is slight rhythmic movement of the forearms, about 60 times a minute. The patient's mind is quite clear for the first time, and he takes an interest in all that is done for him and asks intelligent questions in regard to its purpose. The pulse has ranged from 82 to 96. The temperature (rectal) has been normal. Respirations, 20 to 24. White cells, 9900. Calcium lactate in 1000 c.c. normal salt solution was given.

November 1. The rhythmic movements of the forearms have disappeared. Spasm is entirely absent in the lower extremities. Upper extremities: From time to time the hand is momentarily flexed on forearm at intervals of about five seconds. Mechanical irritation of the nerve trunks does not increase this phenomenon. The calcium salt was omitted and a nucleoproteid preparation of the parathyroid, furnished by Dr. Beebe, was injected deep into the

gluteal region twice in the twenty-four hours. Pulse, 80 to 95 during day. Temperature, slightly subnormal. Respirations, 20 to 24.

November 2. The patient slept quietly during the night. The spasms of the muscles of the forearms have increased and there is very considerable tremor of the hands. There is also some tremor of the muscles of the chin. Pulse, 84 to 96. Temperature, subnormal during the day. Respirations, 20 to 24. In view of the increase in the spasms, in addition to the parathyroid preparation, 4 grams of calcium lactate in 1000 c.c. of normal salt solution was again given intravenously.

November 3. The patient is entirely relaxed and no spasm can be elicited by mechanical irritation of the nerve trunks in either upper or lower extremities or in the muscles of the face. Considerable tremor of the hands is present, however. The patient's general condition is not as good. Hiccough is present. The pulse is of poor force, 80 to 100 during the day. Temperature, subnormal. Respirations, 20. Four grams of calcium lactate in salt solution was given intravenously. From this date the calcium salts were discontinued and no other medication was used. There was no further spontaneous spasm, and it could not be excited by mechanical means. The patient's mind remained entirely clear, he was interested in measures taken for his relief, and was able partially to sit up in bed. There was little or no change in the temperature, pulse, and respirations from those last noted. Three days later, without the occurrence of other symptoms, the heart rather suddenly failed, and death followed speedily.

That portion of the clinical history which especially relates to the tetanic symptoms and to the effect secured by the administration of the calcium salts has been selected for detailed report. Other portions of the history will be given only in outline.

It was found impossible to nourish the patient by means of the stomach. Vomiting was frequent on each attempt, in spite of copious and frequent lavage. Nutriment introduced after lavage by means of the stomach tube, although sometimes retained, was recovered later by the tube in like amounts, showing no signs of gastric digestion—only decomposition processes. Nutrient enemas were only exceptionally retained. There was almost complete anuria for the first twenty-four hours and until abundant subcutaneous clyses of salt solution had been given. Later, the urine either was voided involuntarily or was recovered by catheterization. The scanty fluid stools were mostly involuntary.

Although the tetanic symptoms obviously could be controlled by the continued administration of the calcium salts, it was equally apparent that the patient would slowly die of inanition unless the evident gastric stenosis could be relieved by operation. In consultation, however, my late colleague, Dr. McCosh, decided against surgical intervention, on the ground that any operation would be immediately fatal.

Autopsy, sixteen hours postmortem, by Dr. Opie. The body is that of an emaciated man 160 cm. in length. Over the inner surface of the left elbow and on the right arm there are ecchymoses. The subcutaneous fat is present in very small amount, and has a deep yellow color. The peritoneal cavity contains no accumulation of fluid; fat has almost wholly disappeared from omentum. The greater curvature of the stomach is 16 cm. below the ensiform cartilage in median line. The stomach extends 9 cm. to the right of the midline, and is in contact with the ribs on the left side. The lesser curvature of the stomach in the midline is 6 cm. below the ensiform cartilage. The spleen is firmly adherent to the lateral abdominal wall. The stomach has fallen considerably, and above the lesser curvature the entire head and greater part of the pancreas is visible. The lungs are emphysematous and meet in the median line; a few adhesions bind each apex to the chest wall. The pericardial cavity contains about 10 c.c. of clear fluid. The appendix arises from the inner surface of the cecum, passes inward, and lies with the tip over the pelvic brim. It is possible to pass one finger with difficulty through the foramen of Winslow.

The stomach measures 25 cm. transversely and 8.5 cm. vertically at the cardiac end. Pyloric half is almost tubular and is 5 cm. in diameter. On opening the stomach it was found to contain several hundred c.c. of bright yellow fluid, from which a sediment settles. Adherent to the mucosa is mucus. The mucous membrane is thickened, the rugæ are prominent, and the surface has a homogeneous, deep red color. The wall of the stomach is thickened by hypertrophy of its muscular layer to about 4 mm. The duodenum immediately beyond the pylorus is bent backward and held in contact with the stomach by adhesions for a distance of about 1 cm. Gentle separation of the adhesions exposes a perforation, from which gastric contents escape. It is found impossible to pass a finger from the stomach through the pylorus into the duodenum, obstruction being in a large part due to the bend just described. Immediately below the pylorus in the mucous membrane of the duodenum there is a depressed scar, 0.25 x 1 cm., partially encircling the duodenum. At the upper angle of this area is a deeper ulceration, in diameter not more than 7 mm.; the surface here is black and eroded, and the partial perforation mentioned above allows the passage of a small probe. There is thick fibrous tissue immediately about the ulcer, but no marked induration. The duodenum is somewhat injected, but otherwise normal. The pancreas is normal. The heart weighs 255 grams. The organ is small; the muscle is firm and brownish in color. The aortic valve is normal; there is slight thickening of the free edge of the mitral valve; there are several minute nodular projections. The pulmonary and tricuspid valves are normal. The coronary arteries are smooth.

The left lung is voluminous, and abundant fluid escapes from the

cut surface. Throughout a large part of the upper lobe is scattered gray nodules partly caseous; there are several larger nodules 1.5 cm. across, and cavity formation has occurred in the centre of a caseous area. Right lung is much more voluminous than the left; tubercles are much more numerous in the upper lobe, and there occur several small cavities similar to the cavity in the left lung; it is in direct communication with a bronchus. The uppermost 2 cm. of the apex is almost entirely consolidated by tuberculous nodules. The lower lobe contains sparsely scattered tubercles; in large part it is firm and is partially consolidated by scattered areas of homogeneous, deep red color, though nowhere is it entirely airless. The liver weighs 1450 grams. The organ is firm and deep red; the mottling is indistinct. Gall-bladder is contracted and contains a small amount of viscid bile. The spleen is not enlarged; it measures 11 x 7.5 x 4.5 cm. It is very firm, and has a homogeneous, deep red color; the Malpighian bodies not well seen. The kidneys weigh 310 grams together. They resemble each other closely; the capsule is removed easily, leaving a red surface in which there are a few minute cysts. The cortex, which measures about 5 mm., is deep red. The glomeruli are conspicuous; the pyramids are injected. On the surface of the right kidney there is a yellow patch 0.5 cm. across (apparently aberrant adrenal tissue). Suprarenals together weigh 20 grams. They appear to be normal. The aorta is smooth save for a few slightly raised yellow patches. The urinary bladder is normal in size. Scattered over the inner surface, but chiefly on the posterior wall above the trigon, are submucous hemorrhages; in this situation are numerous minute vesicles. The rectum is deeply injected. The thyroid gland appears to be normal. The two parathyroids on either side were exposed, and as far as could be determined are normal. The small intestine in some places shows injection of the mucous membrane, most marked in the lower part of the ileum where the mucous membrane has a homogeneous, deep red color. The lumen of the appendix is patent. The large intestine throughout shows intense injection of the mucous membrane, but is otherwise negative.

Culture from the heart's blood shows a pure growth of Bacillus coli.

Microscopic Examinations. The liver tissue is much congested. The vessels of the kidney are all dilated and filled with blood. The epithelium of the tubules shows cloudy swelling; the cells are in places desquamated and the tubules are filled with debris. In the cortex there are many areas infiltrated with lymphoid cells. The bloodvessels of the lungs are everywhere congested, and in places there is serous exudate in the alveoli. There are many areas in which the alveoli are completely filled by polymorphonuclear leukocytes; there is a little fibrin. In several areas are chronic tuberculous lesions associated with newly formed fibrous tissue. The

heart muscle is normal. The bloodvessels of the spleen are much congested.

Parathyroid Glands. The right and left superior parathyroid bodies were examined microscopically. They are of normal size and exhibit no abnormality. Scattered cells with affinity for eosin occur in moderate number. There is no increase of connective tissue and the bloodvessels are normal. The right inferior body likewise appears to be normal in structure and size. In the connective tissue near this parathyroid is a small round mass of tissue which resembles the much larger parathyroid body from which it is wholly isolated. The cells which compose this nodule are smaller than those of the parathyroid, and their protoplasm stains more deeply; they are, like those of the parathyroid, arranged in columns between the capillaries. About this nodule connective tissue is concentrically arranged to form an ill-defined capsule; in this tissue lymphoid cells are numerous. At a short distance from the nodule just described, and from the normal parathyroid and situated just outside the wall of a small vein, is an isolated round group of cells identical with those which make up the aberrant nodule. This group consists of about 25 small cells closely packed together. Sections made through the middle of the left inferior glandule showed that parathyroid tissue is abundant and normal. The parathyroid glands therefore, exhibit no abnormality; no evidence of hypertrophy is found. (Near one parathyroid are small aberrant nodules of tissue resembling that of the parathyroid.) The thyroid gland is normal in structure. The alveoli contain colloid in normal amount.

Studies of the Urine. Guinea-pig I. Injected with 20 c.c. of urine into peritoneal cavity. Died after twenty-four hours; some fluid in peritoneum. No exudate. Cultures sterile. Sections, see below.

Guinea-pig II. Injected with 15 c.c. of urine into peritoneal cavity. Died in thirty hours. Findings as in No. I.

Guinea-pig III. Injected with 10 c.c. of urine. Died in thirty-six hours. Findings as above. Three controls using normal urine, all recovered.

Studies of the Stomach Contents. Guinea-pig IV. Given 10 c.c. of filtered stomach contents by stomach tube; after twelve hours looked sick but recovered.

Guinea-pig V. Injected into peritoneal cavity 5 c.c. of filtered stomach contents. Died in ten hours—peritonitis. No convulsions. Cultures showed many organisms.

Guinea-pig I A. Injected 0.1 c.c. into peritoneum. Died in twelve hours. No convulsion. Anaërobic cultures of peritoneum, sterile.

Guinea-pig II A. Injected 0.2 c.c. subcutaneously. After eighteen hours it developed a paralysis of the right fore leg. Became very spastic, especially the hind legs; there was incoördination; no hyper-

esthesia, but stimulation of the abdomen caused clonic contractions of the limbs, which manifested itself in the jumping of the animal in a forward direction, which seemed uncontrollable. On several occasions the animal jumped so high as to strike on the top of the cage. After the spastic stage, a period of great weakness with loss of reflexes ensued, and the animal died in this stage twenty-two hours after injection.

Cultures. Aërobic: heart blood, Bacillus coli(?) spinal canal, Bacillus coli(?) Anaërobic: heart blood, Bacillus coli; spinal canal, sterile.

The abdominal parietes were very œdematous and reddened; no abscess formation; peritoneum and viscera normal. Brain and cord showed no macroscopic lesion.

Guinea-pig III A. 0.5 c.c. injected subcutaneously. This animal showed exactly the same symptoms as No. II A, except that the motor excitement stage was shorter, came on more quickly; died in twenty-one hours.

Cultures: Aërobic, as above; anaërobic, as above. Pathological findings, as above.

The microscopical sections of Guinea-pigs I, II, and III revealed marked cloudy swelling of the viscera; otherwise nothing of note was found.

Filtrate of Stomach Contents (Berkefeld Filter). Injected into guinea-pig as in I A, II A and III A; no apparent effect

Cultures of the filtrate revealed a few colonies of Bacillus coli.

It is a matter of regret that an examination of the brain and cord was not allowed, as the few reports of autopsies in cases of tetany are conflicting both as regards the existence of any constant lesion of the nervous system and its form. The full anatomical report on the parathyroid bodies, by Dr. Opie, is of especial interest.

Certain facts stand out prominently in the clinical study of the case which has been related:

1. The rapid and controlling effect of the soluble calcium salts upon the tetanic symptoms.

2. The maintenance of this effect only by their continued use.

3. The comparatively slight effect of large infusions of salt solutions, used alone.

4. The slight influence, if any, of parathyroid preparations (nucleoproteid) given by the mouth in controlling the hyperexcitability of the nervous system. The effect of the nucleoproteid given subcutaneously cannot be estimated positively in the present instance, as it was given alone only during a period of twenty-four hours and when the tetanic symptoms had been controlled practically by the calcium salt. A distinct renewal of the spasm at the end of this interval led to the renewed use of the calcium salt in combination with the parathyroid material. The demonstration of the controlling influence of the soluble calcium salts upon the characteristic

symptoms of at least one important variety of human spontaneous tetany—the tetany of gastrectasis, with stagnating stomach contents—suggests a probable similar therapeutic value of these salts in other forms of the disease in human beings.

5. The occurrence of typical tetanic spasm in a case of gastrectasis with parathyroid bodies of normal anatomical structure and—presumably—of normal functioning power.

The facts elicited in the clinical and pathological study of the cases add little to our positive knowledge of the pathogenesis of gastric tetany. A profound disturbance of the calcium metabolism would seem probable in the present instance. The explanation of it is difficult. There is much experimental evidence to show that the parathyroid secretion in some way controls the calcium exchange in the body, yet in the present instance the functioning power of the parathyroids presumably was normal. The generation of a poison of unknown nature in such amount as to cause a relative functional inadequacy of the parathyroid bodies can only be a matter of conjecture.

A COMMON MODIFICATION OF THE FIRST SOUND OF THE NORMAL HEART SIMULATING THAT HEARD WITH MITRAL STENOSIS.[1]

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Something like an apology seems due from one who ventures to attribute to trite and familiar phenomena a meaning beyond that which is offered by the consensus of scientific opinion. Yet the adept in auscultation knows that the net value of his examination involves no less the neglect of adventitious sounds than the appreciation of those which are of diagnostic worth. Therefore physical signs which pass unnoticed because devoid of meaning at once attract attention when they are found to imply an important modification of vital activity.

It is the design of the present contribution to direct attention to a modification of the first sound of the heart which allies it qualitatively to the first sound as heard in mitral stenosis, but which predicates no organic lesion. I venture to suggest that the light recently thrown by physiologists on the nature and variations of blood flow within the normal heart may be directed to the illumi-

[1] Read by title at a meeting of the Association of American Physicians, Washington, D. C., May 11 and 12, 1909.

nation of certain clinical signs which are ordinarily disregarded, because not significant of organic disease.

The tone of the normal first heart sound is distinctly decrescendo in character; the accent is at the beginning of the sound. In the simplest typical case of mitral stenosis the tone of the first sound is crescendo-decrescendo; the most striking moiety of the sound being formed by its initial acute accent. By clinical inference the crescendo element of this sound is presumed to precede contraction of the ventricle and to be therefore presystolic in time. It is further designated as a "murmur," and is thereby at once genetically separated from the normal heart sounds. This topic will rest with simple reference to the fact that the pathological presystolic murmur may pass by insensible gradations from a sound of indefinite duration and extreme roughness of quality to one indistinguishable in quality from the normal first sound and only of sufficient duration to give a crescendo accent to the latter.

The clinical thesis here maintained is that, though the heart may have normal valves, its first sound may begin with the crescendo tone and thus assume the essential character of the sound as heard in mitral stenosis. It must be premised that such a modification of the normal first sound is found only in cases in which the general clinical condition signifies either essential cardiac weakness or perturbation due to acceleration of the circulation; this acoustic phase is therefore of distinctly diagnostic worth.

The crescendo tone of functional origin which may initiate the first heart sound varies considerably in quality, duration, and intensity. Most commonly it occurs as an extremely short, smooth tone, with an acute accent apparently sharply terminating with the beginning of ventricular contraction. Precisely this modification of the first sound of the heart is frequently the sole auscultatory sign of organic mitral stenosis when, presumably, the contractile energy of the left auricle is slight. The first sound as a whole often acquires, in the normal heart, a remote suggestion of the snapping first sound in mitral stenosis. It is not uncommon for the clinical observer to witness, in a given case from day to day, the presystolic murmur of organic mitral stenosis to vary insensibly from a most exaggerated and palpable vibration to a tone which has little intensity and scarcely perceptible duration, and which barely gives the impression of an acute accent initiating the first heart sound. On the other hand, postmortem examination has shown me the heart valves to be normal in cases in which, during life, the crescendo character of the first sound had been so pronounced as to lead to the suspicion of organic mitral obstruction. In other cases of what may be called the "functional presystolic murmur," the crescendo tone is rough and vibratory in character and of perceptible duration. No examples of this category have come to autopsy, but numerous cases have been noted in which the

auditory signs alone strongly suggested organic mitral stenosis, but in which the general signs of the disorder were lacking. One other presystolic auditory symbol, closely allied to the latter, is found in certain of the so-called "reduplications" of the first sound of the heart. When such a "reduplication" is the weaker of the two elements and precedes the contraction of the left ventricle without a perceptible intermission, the first sound may appear to begin with a crescendo tone. It may be said, in passing, that any explanation that holds for the production of the presystolic functional "murmur" would probably denote the origin of at least certain common reduplications of the first sound.

The above is a brief expression of clinical facts as they appear to me. The subject seems worthy of attention, because, first, there is often real difficulty in distinguishing clinically the presystolic sound due to organic valvular stenosis from that arising from functional causes, and second, a consideration of recent disclosures as to the mode of filling of the normal heart seems to suggest an explanation for the functional quasipresystolic murmur which makes it of diagnostic value. The following considerations are offered with a view of elucidating the subject.

The elements entering into the production of the first sound of the heart, especially when there exists obstruction at either auriculoventricular orifice, are exceedingly complex. The characteristic crescendo murmur of mitral stenosis is, according to accepted clinical teaching, produced by vibrations caused by the stream of blood ejected by the contracting left auricle. The murmur is therefore presystolic in time as regards the cycle of the ventricle. Yet, according to the admirable resume of the subject by Gibson,[2] several competent observers maintain that the murmur in question is produced by contraction of the ventricle only, ceasing at the moment of valve closure, and is therefore "systolic" or "protosystolic" in period. Without discussing this discrepancy of opinion, I will assume as correct that view which attributes the presystolic murmur of mitral stenosis to vibrations in the mitral valve and blood current produced by the systole of the left auricle. It only remains to recall the well-known fact that, without evidence of change in the degree of stenosis, the presystolic murmur in a given heart completely disappears either as a result of an exaggerated break in compensation or even, at times, when functional efficiency has been restored. In the first case the loss of the murmur is attributable to paralysis of the left auricle; in the second, to a recovery of the normal balance of pressures in the cardiac chambers.

In 1862[3] Austin Flint described a presystolic murmur as occasionally occurring in subjects suffering from uncomplicated insuffi-

[2] Diseases of the Heart and Aorta, 1898, p. 157.
[3] Amer. Jour. Med. Sci., 1862, xliv, 29.

ciency of the aortic valves while the mitral leaflets remained normal. Flint's description was so convincing that the murmur has commonly been designated by his name. As observed by Dock,[4] German writers commonly ignore Flint's contention, while, on the other hand, in a critical review of the subject, Thayer[5] concludes that "one may be justified in saying that in uncomplicated aortic insufficiency a rumbling, echoing presystolic or mid-diastolic murmur limited to the region of the apex of the heart is very common, occurring, when carefully looked for, in fully half of the cases. The characteristics of this murmur are in no way different from those commonly observed in true mitral stenosis, with the exception of the fact that it is usually of moderate intensity."

In explanation of the origin of his murmur, Flint, as quoted by Thayer, writes: "Experiments show that when the ventricles are filled with a liquid the valvular curtains are floated away from the ventricular sides, approximately to each other and tending to closure of the auricular orifice. In fact, as shown by Drs. Baumgarten and Hamernick, of Germany, a forcible injection of liquid into the left ventricle through the auricular opening will cause a complete closure of this opening by the coaptation of the mitral curtains, so that these authors contend that the natural closure of the auricular orifices is effected not by the contraction of the ventricles, but by the forcible current of blood propelled into the ventricles by the auricles. However this may be, that the mitral curtains are floated out and brought into apposition with each other by simply distending the ventricular cavity with liquid is a fact sufficiently established and easily verified. Now, in cases of considerable aortic insufficiency, the left ventricle is rapidly filled with blood flowing back from the aorta, as well as from the auricle before the auricular contraction takes place. The distention of the ventricle is such that the mitral curtains are brought into coaptation, and when the auricular contraction takes place the mitral direct current passing between the curtains throws them into vibration and gives rise to the characteristic blubbering murmur. The physical condition is, in effect, analogous to the contraction of the mitral orifice from an adhesion of the curtains at their sides, the latter condition, as clinical observation abundantly proves, giving rise to a mitral direct murmur of similar character."

It is not difficult to simulate on the excised heart the conditions premised by Flint, as has been demonstrated to me by Dr. A. D. Hirschfelder. When the left auricle is cut away and the left ventricle is distended with water through a tube tied in the aorta, the mitral valves float up and are closely coaptated. If, now, water be poured from a height upon the upper surface of the valve, simu-

[4] Nothnagel's System of Medicine, Translation, Diseases of the Heart, p. 373.

[5] Observations on the Frequency and Diagnosis of the Flint Murmur in Aortic Insufficiency, Trans. Assoc. Amer. Phys., 1901, xvi, 393.

lating the effect of auricular contraction, it will be seen that the mitral curtains are not forced apart throughout their whole line of contact, but are only separated for a fraction of it in a way to imitate the mechanical conditions of mitral stenosis. Most authors now admit the occasional occurrence of Flint's murmur, though most diverse opinions prevail as to its cause. An extreme example of dissent from Flint's explanation of the origin of the murmur is furnished by Gibson[6] who writes: "The opinion expressed by Flint is of course absolutely untenable. No one with any knowledge of the physiology of the intracardiac movements could for one moment uphold it." Nevertheless, it is just this opinion on which I venture to found the tenets of this paper.

The recent admirable investigations of Hugh A. Stewart[7] have thrown doubt upon all preconceptions as to the modification of intraventricular blood pressure as influenced by aortic insufficiency. Stewart experimentally ruptured the aortic valve in anesthetized dogs while recording, at the same time, the course of arterial blood pressure and volume changes in the ventricles. Stewart maintains that the volume of blood which regurgitates as a result of aortic insufficiency "is negligible." "When the insufficiency is extensive, the pressures in the aorta and ventricle become equalized during the period of relaxation, and there is no further transmission in the phase of ventricular diastasis," that is, during the period of fixed diastolic distention. When, however, the aortic lesion is slight, it is possible, says the author, that the aortic pressure may cause the pressure in the ventricle to rise during the whole period of diastole. Such variations of intraventricular pressure resulting from similar lesions may readily account for the divergence in clinical signs.

Our conceptions of the intracardiac circulation have been greatly illuminated by the now familiar researches of Yandell Henderson[8] whose conclusions have been essentially confirmed by Stewart and by Hirschfelder.[9] Henderson enclosed the ventricles of the living dog's heart within a rubber ball, the organ being inserted through an aperture whose rim could be made to fit accurately the auriculo-ventricular groove. The cavity of the ball being in connection with a tambour, the volume changes of the ventricles were registered with exactness.

The study of his tracings led Henderson to the deduction that the ventricular cycle is composed not, as usually taught, of two, but of three distinct phases, namely, *systole*, or period of contraction and emptying; *diastole*, or period of relaxation and filling; and *diastasis*, or period of rest. He insists that the act of relaxation or diastole is

[6] Op. cit., p. 501.

[7] Experimental and Clinical Investigation of the Pulse and Blood Pressure Changes in Aortic Insufficiency, Arch. Int. Med., 1908, i, 102.

[8] The Volume Curve of the Ventricles of the Mammalian Heart, etc., Amer. Jour. Phys., 1906, xv, 325.

[9] Johns Hopkins Hosp. Bull., November, 1908.

almost or quite as rapid as the systole; "the refilling of the ventricles occurs early in diastole; . . . it is as rapid a process as is the systolic emptying." Following the phase of what may be called active relaxation comes the period of diastasis. "During this period there may be no further relaxation of the ventricles if the number of beats executed in the few seconds preceding has been few, and the tonus is therefore slight. If, however, the beats have been occurring in rapid succession, there may be a gradual relaxation throughout this period as the tonus thus induced gradually wears off. This period (diastasis) is of extremely variable duration." When the rate of heart beat quickens, the increase is due to shortening of the phase of diastasis; when the beat is slowed, it is by prolonging diastasis. "Auricular systole plays a part which is mechanically of very minor importance in the normally beating heart. . . . The mammalian auricles are to be regarded as elastic reservoirs rather than as force pumps. When the dog's heart is beating at a slow natural rhythm the ventricles are refilled so rapidly after each discharge that a period of quiescence may intervene after the refilling is completed, and before the onset of auricular systole. Under such conditions the auricles inject only a small fraction of a cubic centimetre of blood into the already distended ventricles. The currents in the blood thus induced may cause the closure of the auriculoventricular valves. Except for this possible effect, auricular systole is a factor of almost negligible dynamic value." It would seem hard to overestimate the importance of this assumed effect of auricular contraction on the mechanical perfection of valve closure at the outset of ventricular systole. According to Henderson, at slow normal rhythms the ventricles are not completely emptied at systole, but still contain from 20 to 30 per cent. of their diastolic volume. As the heart beat quickens, the tonus of the muscle increases, the ventricle relaxes less in diastole, but an identical volume of blood is ejected at each systole because of more complete contraction of the organ. The optimum rate of beat, through which the maximum amount of blood is discharged within a given time, is a rate at which the ventricle contracts as soon as it is filled, and in which the period of diastasis is completely eliminated. A further increase of rate must diminish the total output, because each systole supervenes upon an incomplete diastole. Admirable researches by Thayer[10] and by Hirschfelder[11] have demonstrated the extreme probability of a frequent diastolic closure of the auriculoventricular valves, brought about by the reflux of the inflowing stream. The view is advanced that this closure is effected with sufficient energy to produce an occasional "third heart sound."

[10] On the Early Diastolic Heart Sound (the so-called Third Heart Sound), Boston Med. and Surg. Jour., 1908, clviii, 713.

[11] Loc. cit.

Students of the venous pulse are familiar with a wave, common in tracings from somewhat weak hearts, just preceding the wave made by auricular contraction. Such a wave could probably be produced by sudden uplift of the auriculoventricular valves.

Now, with all these facts in view, the imagination is compelled to conceive a series of valve movements which may well give rise to modification of the normal first sound of the heart. If, for example, the heart is beating near its optimum rate, the inrush of blood into the ventricles during diastole may be supposed more or less completely to approximate together by its reflux currents the auriculoventricular curtains, much as, according to accepted theory, they are coaptated by auricular systole at the end of the normal period of diastasis. But in the hypothetical case the auricles contract at the moment when the auriculoventricular valves are being actively urged upward by the reflux of blood entering the ventricle during its diastole. In such a mechanical situation the auricular stream would presumably find for itself a place of least resistance of relatively small caliber between the valve curtains, traversing which the fluid and the valve would be thrown into vibrations essentially similar in origin and period to those characteristic of mitral or tricuspid stenosis. It is obvious, also, that the modification of the first sound of the heart thus produced, while perceptible as a presystolic crescendo phase, would rarely be obtrusive, but require for its detection the conscious attention of the examining ear.

SUMMARY. In the structurally normal heart, especially in conditions of circulation excitement, the first sound frequently begins with a crescendo tone, simulating closely the faint and brief presystolic murmur or acute accent initiating the first sound in certain stages of organic mitral stenosis. This modification of the first sound may be pronounced either in the tricuspid or the mitral area or both. An attempt has been made to show that when the ventricles are filled at a certain rate the reflux of the blood current may be expected to bring the auriculoventricular valves sufficiently into approximation, so that the auricles in contracting must force a channel between them and cause vibrations of perceptible intensity, thus giving rise to an audible presystolic tone or murmur.[12]

[12] After this article was in type, a reference was found to a dissertation by Perlis (Practical Medical Series, 1909, i, 174), in which it is maintained that a functional presystolic murmur due to inorganic mitral stenosis may be heard in certain diseases and conditions.

GASTRO-INTESTINAL AUTO-INTOXICATION.[1]

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It seems a well-established fact that products of intestinal putrefaction, when absorbed without being properly changed or destroyed by the antitoxic activity of the intestinal wall and particularly of the liver, may cause systemic disturbances. On the other hand, it must be said that there is a general tendency at present greatly to overestimate the role which gastro-intestinal toxemia plays in the development of certain diseases. The fashion of the day, following the teachings of the French school, attributes to gastro-intestinal intoxication various diseases of the nervous system, the circulatory system, the blood, the muscles, the skin, etc. When, however, we examine the arguments which are given to prove the intestinal autotoxic origin of most of these diseases, it is astonishing to find how very few reliable facts gained by experimental research, by exact chemical investigation, or even by accurate clinical observation, have so far been advanced to support this theory for each case. While the occurrence of gastro-intestinal auto-intoxication has undoubtedly been demonstrated for some conditions, the application of this theory to numerous diseases merely on the strength of analogy has led to a great confusion of the whole question, particularly in regard to the magnitude of the role which intestinal intoxication plays in different diseases.

I have no intention of discussing in this short paper the different aspects of this difficult topic; I must confine myself to a few general remarks.

Under the heading of toxemias of gastro-intestinal origin are commonly included all intoxications which can be ascribed to the absorption of toxic substances formed in the alimentary canal by the action of digestive ferments or of bacteria. These endogenous intestinal intoxications are distinguished from so-called exogenous intoxications, which are principally caused by the taking of decomposed food. Together with this decomposed food, products of protein putrefaction, especially of the ptomain type, are usually ingested and thus act as severe poisons. It seems, however, that in a number of cases of apparent ptomain poisoning, the severe symptoms are not caused by the action of poisons formed in the food before it was eaten, but by the effect of intestinal infection of this food by bacteria, mostly of the paratyphoid type, so that these cases of apparent exogenous auto-intoxication are actually cases of endo-

[1] Read at a meeting of the New York Academy of Medicine, Section on Medicine, December 15, 1908.

genous auto-intoxication. Whether these and other severe pathogenic intestinal infections lead to the formation within the intestinal canal of such bodies as ptomains has not yet been definitely proved. There can be no doubt, however, that intestinal infections of this kind produce toxic substances the absorption of which causes more or less severe systemic disturbances, although as yet no such substances have been isolated.

One meets with other conditions in which the resemblance of the clinical picture to that of ptomain poisoning suggests that they are caused by the action of intestinal toxins. I refer to the well-known attacks of sudden and uncontrollable vomiting with extreme ababdominal pains and serious vasomotor disturbances, for which exogenous intoxication can be excluded and no other cause is found. These attacks, by the way, sometimes end fatally. There is, however, the possibility that these are cases of metabolic, not of gastro-intestinal auto-intoxication.

Again, in acute intestinal obstruction some of the violent symptoms are very probably due to the activity of highly toxic substances formed in the alimentary canal. In chronic intestinal obstruction such symptoms as fever, albuminuria, and severe disturbances of the nervous system indicate the possible action of enterotoxins. Among the nervous syndromes observed in cases with obstruction in the alimentary canal, I have to mention the form of tetany which occurs with gastric ulcer and pyloric stenosis. Gastric tetany is often pointed out as one of the most striking illustrations of toxemia caused by the absorption of toxic substances from the dilated stomach. This positive statement is not well supported by facts.

Some years ago I offered another possible explanation for gastric tetany with pyloric obstruction.[2] I argued that it is caused by an impoverishment of chlorides in the system, which is brought on through the constant loss by vomiting and lavage of great quantities of chloride with the highly acid gastric secretion. This theory, that the attacks are caused by the loss of a constituent necessary to the intermediary metabolism, and not by the toxic effect of a substance absorbed from the stomach, is well corroborated by experiments. According to Taylor[3] tetanic seizures are observed in dogs in whom the duodenum is cut across and the ends brought into external fistulæ, so that the gastric contents leave the body and its constituents fail to return to the circulation by intestinal resorption. It is possible that different and perhaps more satisfactory explanations may be found for other diseases, in which some features of the clinical picture suggest the effect of intestinal intoxication. I mention for such examples, tetany of children suffering from diseases

[2] Gastrosuccorrhea and Tetanic Attacks Occurring with Chronic Ulcer of the Stomach, AMER. JOUR. MED SCI., April, 1904.

[3] Osler's Modern Medicine, vol. i, p. 277.

of the digestive tract, also certain skin eruptions, notably when occurring with pronounced gastro-intestinal disturbances, such as vomiting, diarrhœa, etc.

In some conditions it is the resemblance of the symptoms to those brought on by the known effect of poisons which justifies the assumption of intestinal intoxication. In no disease has this been demonstrated with more clearness than in cases of pernicious anemia. The investigations of Dr. Herter[4] have greatly added to our knowledge of the intestinal processes connected with such cases. The fact itself, that in a group of cases of pernicious anemia the hemolytic substances originate and are absorbed from the digestive tract, was known for some time. It was proved long ago for patients who harbored Bothriocephalus latus, but it was also recognized in cases in which no such higher parasites were present. I may mention here, that about twenty years ago, while still an assistant at Kussmaul's clinic, I discussed this topic in an article reporting a case of pernicious anemia, caused by chronic gastro-intestinal disturbances and cured by appropriate treatment.[5]

In other conditions which are usually attributed to intestinal intoxication the characteristic symptoms are not such as to suggest intestinal intoxication as the most probable cause for their development. In asthma dyspepticum, for example, the direct mechanical effect of the gas-distended abdominal viscera, usually found in these cases, and the effect of nervous reflex action, offer a much more plausible explanation. The fact that the attacks occur in connection with digestive disturbances and disappear with their improvement does not throw any light upon their assumed toxic character. The same may be said of numerous other conditions looked upon as intestinal toxemias, particularly diseases of the nervous and circulatory system, the skin, etc.

It is true that digestive disturbances provoke epileptic attacks, and that the treatment of such disturbances, especially the proper care for regular evacuation of the bowels, reduces, perhaps more than any other form of treatment, the number of attacks. Yet the good effect of such treatment itself is not sufficient to show that the digestive disturbances are the primary cause of the epileptic condition, and still less that this is effected by the action of toxins of intestinal origin.

I am far from underestimating the importance of digestive disturbances in the development of diseases of other organs. For some diseases we have a rational explanation other than autotoxic which makes us understand the causal connection between digestive and other systemic diseases. In other conditions this causal connection is still obscure. The fact that we do not know the cause does

[4] Jour. Biol. Chem., August, 1906; Bacterial Infections of the Digestive Tract, 1907.
[5] Zwei Fälle geheilter perniciöser Anämie, Berl. klin. Woch., 1890, No. 10.

not justify the present tendency to consider these diseases as principally caused by intestinal intoxication. If we are to accept this theory, we should be convinced by the demonstration of sufficient direct evidence in each instance. It should further be shown whether intestinal intoxication, when present, is a primary or only a secondary cause, and how great a role it plays in the pathogenesis of each condition.

Before discussing the direct evidence generally offered, it should be said that it is the same for conditions of distinct digestive disturbances as for those in which no gastro-intestinal symptoms at all, or only constipation, is present. The evidence consists principally of the appearance in the urine of products of intestinal bacterial disintegration. However, products of intestinal putrefaction are not the only substances accused of acting as toxins. It is further claimed that products of digestion, and even the digestive fluids themselves, may eventually have a toxic effect upon the system, when absorbed without being changed by the antitoxic activity of the intestinal wall and the liver. To dispose of the digestive fluids and the products of digestion first, I quote Taylor,[6] who, in his excellent article on this topic, states that there is not a single reported experimental or clinical fact which is explained by the assumption of the resorption and non-distoxication of the digestive juices; nor has it been shown that the products of normal digestion ever act as toxins.

We may now turn to the substances formed by the action of bacteria within the alimentary tract. The products of fermentation of carbohydrates, the acids, are, on the whole, harmless; increased in quantity (or with irritable organs in moderate amounts), they form a local irritant, causing vomiting or diarrhœa. When absorbed they are readily oxidized in the body; it is possible, however, that when formed in excessive quantities and quickly absorbed, they may lead to acid intoxication by robbing the system of great quantities of alkali. Acidosis observed in infantile enteritis is considered by some as of intestinal origin; others maintain that acidosis is always of metabolic origin, in this as well as other instances. Lactic acid, with bacterial gastric fermentation, seems to be well tolerated even when produced in large quantities. I had occasion to observe for a long period the unusual case of a very pronounced non-carcinomatous bacterial fermentation of the stomach, with constant production of great quantities of lactic acid, in which no symptoms appeared which pointed to toxemia. Of products of fat decomposition, cholin derived from lecithin is declared a highly poisonous compound, and it is said that some of the ill effects observed after eating excessively of such foods as eggs or calves' brains may depend upon the toxic

[6] Osler's Modern Medicine, i, 270.

action of cholin.[7] More weight is attributed to the products of intestinal putrefaction of proteins, which are chiefly held responsible for intestinal toxemia. A certain amount of bacterial disintegration of proteins in the intestines is normal. Normal is also the finding in the urine of a certain amount of those substances by which the degree of intestinal putrefaction is measured, that is, the ethereal sulphates and indican.

Estimation of the ethereal sulphates is a more reliable method of determining the degree of intestinal putrefaction. But since the indican reaction is the only test available to the general practitioner, it is very extensively used as an index of intestinal protein putrefaction, and the finding interpreted as a sign of auto-intoxication. In discussing the value of the indican test, it should first be stated that with adults living on a mixed diet a positive indican test is the rule. For a number of years I have examined systematically every urine of adults for indican and the cases in which the test was negative were very rare. The amount varies; it does not depend exclusively on the degree of intestinal putrefaction, but also on the degree of its absorption and other factors, so that there is no constant relation between the output of indican and the degree of intestinal putrefaction. As a rule, however, an outspoken excess of indican points to an increased intestinal putrefaction of proteins. The same considerations apply to an increase of ethereal sulphates.

I shall abstain from discussing the different conditions which may account for an excessive output of indican and of ethereal sulphates. In taking an increased intestinal putrefaction as its principal cause, I shall proceed to the questions: (1) What information do we obtain from the finding of increased intestinal putrefaction in regard to intestinal intoxication? (2) How far are we justified in interpreting excess of indican in the urine as a sign of intestinal intoxication? At present it is very difficult to answer these questions exactly. We have only to consider different possibilities.

Increased intestinal putrefaction may cause an increase of the known normal products of putrefaction, and it may lead to the formation of other new products of toxic character. It is often assumed that with increased intestinal putrefaction new substances are formed, which may possibly act as toxins. As long as such hypothetical substances have not been demonstrated it is of questionable value to estimate their presence and quantity by measuring the degree of intestinal putrefaction in general. The mere presence of such substances in the feces would not mean anything in regard to their toxic effect upon the system, because they may be detoxicated after absorption. All efforts, however, to find such enterotoxins in the urine have so far failed.

Especially the determination of the so-called urotoxic co-efficient

[7] Quoted from Wells, Chemical Pathology, p. 480.

cannot be considered a reliable method of diagnosticating the presence of enterotoxins in the urine, and still less of measuring their quantity. In regard to the known products of gastro-intestinal putrefaction, it must be said that according to our present knowledge, only few are toxic to any considerable degree, and these are produced in too small quantities to cause any appreciable effect.

Only for one product, for hydrogen sulphide, has it been demonstrated that it may be formed and absorbed in such quantities as to cause symptoms of intoxication. Such cases, first described by Senator[8] as hydrothionemia, are very rare; so are the cases described by Stokvis[9] as enterogenic cyanosis, apparently caused by the action of hydrogen sulphide of intestinal origin on the blood. These are characteristic clinical pictures of intoxication, which may be excluded from our general discussion on the diagnostic value of the excessive output of indican and the ethereal sulphates.

Of the other products of intestinal putrefaction, neither indol nor skatol, nor the sulphurous bodies and the amino-acids, are toxic to any considerable degree. Even an excess may be tolerated, as is shown by the observations that some individuals, who are otherwise healthy and show no signs of intoxication, eliminate very large quantities of indican and ethereal sulphates. It has been claimed that the same products of intestinal putrefaction, which are comparatively innocuous under ordinary circumstances, may become toxic under other conditions, especially when acting over a longer period. Herter,[10] for instance, maintains that in certain diseases the liver and other cells most concerned in oxidation show less ability to oxidize indol and to pair it with sulphuric acid, thus forming indican. He further claims that free indol has a toxic influence upon the neuromuscular system, and that this effect accounts for the development of such diseases as myasthenia gravis. Without discussing the merits of this theory, which has not yet been verified by the demonstration of free indol in the blood or in the urine, it must be stated that the excessive output of indican observed in such cases does not speak in favor of the assumed action of free indol. On the contrary, the finding of great quantities of indican shows that the pairing of the indol has been very satisfactorily perfected. This and similar considerations make it clear that excess of indican of itself is not sufficient to diagnosticate intestinal toxemia. Neither the indican test nor the estimation of the ethereal sulphates furnishes direct evidence that substances absorbed from the alimentary canal act as toxins. An excessive output of these bodies merely indicates that more protein than usual is undergoing putrefaction. This increased putrefaction may be innocuous. However, it must be admitted as possible that,

[8] Ueber Schwefelwasserstoff im Harn, Berl. klin. Woch., 1887.

[9] Zur Casuistik der autotoxischen enterogenen Cyanosen, Festschr. f. v. Leyden, 1902, p. 597.

[10] Bacterial Infections of the Digestive Tract, chapter on Indol and Indicanuria, 1907.

under certain conditions, products of increased intestinal putrefaction may cause systemic disturbances.

Finding so far no direct evidence, we have to turn to characteristic clinical symptoms for an indirect support of this theory.

In some disease we again find the only available support in the analogy to the effects of other known toxins, for instance, in neurasthenia. In neurasthenia we are familiar with an increased susceptibility to exogenous toxins like alcohol, tobacco, etc. It is assumed that a like increased susceptibility exists for the toxic effect of products of intestinal putrefaction, which under ordinary circumstances are well tolerated by the system. Taking this for a correct view, it would only show that the toxic effect of intestinal products may aggravate the neurasthenic condition. But it cannot be taken as an argument for the claim of some writers, that intestinal intoxication is an important primary cause of neurasthenia. I agree with those who consider heredity, worry, overwork, etc., as primary causes of neurasthenia. The increased susceptibility for toxins forms already part of the neurasthenic condition. Since digestive disturbances are often associated with neurasthenia, the effect of increased intestinal putrefaction may prove deleterious in creating a vicious circle. Similar considerations apply to the relation of digestive disturbances to other diseases of the nervous system.

Among the symptoms often quoted as characteristic of intestinal intoxication I have to mention albuminuria. The kidneys are very sensitive to poisons, and albuminuria occurs regularly when poisons are passed by the kidneys. Since albuminuria is a frequent symptom with diseases of the alimentary tract, it seems justified to attribute this to the effect of passing intestinal toxins. This may be, and certainly is, correct for some conditions, but not for all. From my own observations I have come to the conclusion that in one distinct group of digestive disturbances albuminuria is caused by increased acidity of the urine, with and without uric acid or oxalic acid sediment. When, in these cases, alkalies, especially preparations of magnesia, are administered in such quantities that the urine becomes slightly alkaline, the albumin disappears, to recur again with renewed increased acidity. In one of my patients I have been able to verify this numerous times during the course of years. In these cases, therefore, albuminuria is not caused by the direct action of enterotoxins on the kidneys, but by the effect of products of disturbed metabolism.

This leads us to a different aspect of toxemias connected with diseases of the digestive tract. Gastro-intestinal disorders often interfere with the activity of the liver, thereby disturbing the normal processes of metabolism. The manifold results of disturbed metabolism, symptoms of uric acid diathesis, the development of diseases of the kidneys, the arteries, the heart, etc., are often described as caused by the action of toxins of intestinal origin. If by the term

gastro-intestinal toxemia we mean the intoxication caused by the action of substances absorbed from the alimentary canal, then these are not cases of gastro-intestinal but of metabolic toxemia. Metabolic derangement may be instituted by gastro-intestinal disorders, but it may have other etiological factors, as mental strain and other disturbances of the nervous system.

It is necessary to distinguish strictly between gastro-intestinal toxemias and metabolic toxemias, especially at present, when Metchnikoff's ideas have taken such a hold on laity and profession, and when it is almost taken for granted that the so-called antifermentative treatment of digestive disorders is the most important and the most effective way of dealing with chronic systemic diseases.

Effective treatment of gastro-intestinal disturbances is certainly of great importance in systemic diseases. But I doubt very much whether this difficult task can be accomplished when the plan of treatment is based on the theory that the action of enterotoxins is at the bottom of it all. The fascinating theory of gastro-intestinal toxemia is in most instances still very much in need of support by objective facts. If we wish to gain more evidence and to clear up the many questions connected with this theory, we must show a more critical attitude than is generally displayed at present.

ACQUIRED CHRONIC ACHOLURIC JAUNDICE, WITH A BLOOD PICTURE AT ONE TIME RESEMBLING THAT OF PERNICIOUS ANEMIA.

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The patient, Mrs. L. P., now aged thirty-eight years, was admitted under my care at the German Hospital in January, 1908, with blood changes characteristic of pernicious anemia, and on April 13, 1908, she was shown at the Medical Society of London as a "Case of Enlargement of the Spleen and Liver with Pernicious Anemia." She was again shown at the same society on February 8, 1909.

Up to the time of admission the history was that the patient had previously been healthy. About three years back she began to get paler, and about a year later she had an attack of deep jaundice (with pains in the right side), which was followed by dropsy. After that she gradually became weaker and paler and short of breath on exertion. Menstruation became scanty, and for a time there was complete amenorrhœa. She suffered from recurrent epistaxis.

She was troubled with coldness and numbness of the hands and feet; sometimes she had a sensation of pins and needles in the fingers, which would often "go blue."

In regard to the family history it was to be noted that her mother had died of liver disease, aged fifty-two years. The patient herself was a widow, who had been married twice. By her first husband she had two children, the first one born dead, the second one still living and healthy. By her second husband (who was addicted to alcohol) she had no children.

After admission to the hospital the condition noted was the following: The skin and conjunctivæ were yellowish. There was no pruritus or xanthoma. The legs were œdematous. The heart seemed slightly dilated, and there was a faint systolic murmur, apparently not due to valvular disease. The liver and spleen were both evenly enlarged. The liver extended two or three finger breadths below the ribs, and the spleen, which was hard, reached almost to the anterior superior iliac spine. The condition of the patient's mouth was not bad, though she had lost many of her teeth. Occasionally there was slight bleeding from the gums. Attacks of epistaxis were frequent. Ophthalmoscopic examination (Dr. C. Markus) showed numerous bright red, round, retinal hemorrhages in both eyes, chiefly in the upper halves of the fundi. The urine, of specific gravity 1013, contained albumin (1 per mille by Esbach's tube on admission), but no tube-casts. A later note of the urine stated it to be of specific gravity about 1015, of deep orange color, free from albumin and sugar, and giving no Gmelin's reaction for bile pigment, but containing excess of urobilin. The feces were never acholic.

Examination of the blood on January 31, 1908, gave the following result: Hemoglobin (by Haldane's method), 18 per cent.; red corpuscles, 900,000 in the cubic millimetre; white corpuscles, 6000; color index, 1. From a preparation of the same date Dr. A. E. Boycott made the following differential count of 500 white cells: Lymphocytes, 45.6 per cent; intermediates, 4.8; large hyalines, 2.4; neutrophile polymorphonuclears, 46; eosinophiles, 0.8; mast-cells, 0.4. During the count of 500 white cells he saw no ordinary normoblasts, but eight typical megaloblasts (that is to say, megaloblasts with cytoplasm staining as in the typical megaloblasts of pernicious anemia) and 16 smaller nucleated red cells resembling the typical megaboloblats except in regard to their relatively small size. There were a few polychromatophilic red cells and many punctate basophilic red cells. Poikilocytosis (as to shape and size of the red cells) was characteristic for pernicious anemia. No myelocytes were seen. An examination (May, 1908) of the contents of the stomach one-hour after a test breakfast consisting of dry bread and tea showed the absence of free hydrochloric acid.

The treatment in the hospital consisted chiefly of rest (at first rest

in bed), subcutaneous injections of the arsenic preparation, known as atoxyl, chalybeate medicines by the mouth, and acid glycerin of pepsin after meals. The amount of atoxyl injected was usually 0.1 gram (that is to say, 1 c.c. of a 10 per cent. solution) twice weekly. Calcium lactate was occasionally given on account of urticaria and subcutaneous hemorrhages. For about a week in September inunction of the splenic region with an ointment of the biniodide of mercury was tried, but with no definite result. The atoxyl treatment was commenced very soon after the patient's admission in January, 1908. It was continued with intervals till July 21, 1908, and then discontinued.

The patient has been over a year in the hospital. Progress was for a long time very slow and rather unsatisfactory, but decided improvement was observed in November, 1908, and has continued since then. The patient now feels and looks almost quite well. She has long been allowed to get up. She is free from jaundice, fever, and œdema and has gained considerably in body weight (133½ pounds in February, 1909, as compared with 118¼ pounds in February, 1908). The blood shows only slight anemia. The heart is not dilated, and shows nothing abnormal except a very slight systolic murmur best heard in the pulmonary area. The pulse frequency is 82 to 96 in the minute. The brachial systolic blood pressure is 100 mm. Hg. The spleen can only just be felt. The edge of the liver cannot be felt, though the organ is still probably somewhat enlarged. The retinæ are free from hemorrhages, but the patient continues to suffer from attacks of epistaxis at short intervals. Menstruation has recently recommenced, after a prolonged period of amenorrhœa. The stomach contents after a test meal show the presence of free hydrochloric acid. There is no excess of urobilin in the urine and the blood serum (kindly examined by Dr. Leonard Dudgeon on November 25, 1908) is free from bile pigment.

Several features of the patients' illness require special mention and consideration.

Abdominal Pain. At various times the patient has complained of pain or tenderness in the upper part of the abdomen, sometimes in the region of the liver, sometimes associated with fever. An attack about the middle of August, 1908, was associated with vomiting and temporary increase of the icteric tinge; a short attack in December was accompanied by a sudden rise of temperature to 103° F.

Jaundice. While under observation the patient was never deeply jaundiced, but the conjunctivæ for a long while were distinctly yellow. With the improvement in the general condition in November the jaundice entirely disappeared, and has not reappeared since. With a single doubtful exception (during a temporary exacerbation of the jaundice), bile pigment was never present in the urine; the feces were never acholic.

Temperature. At first there were recurrent periods of moderate fever, but since September there has been hardly any. The last occasion on which any fever occurred was on December 13, when a temperature of 103° F. was noted in association with abdominal pain.

Retinal and Other Hemorrhages. The retinal hemorrhages noted by Dr. C. Markus were peripheral in distribution, and chiefly in the right eye. They temporarily disappeared in the early part of April, 1908, but were noted again at the end of the month and in August and September. There are none to be seen at present. Recurrent attacks of epistaxis have been a feature throughout the illness. They still occur at short intervals, but for several months she has had no bleeding from the gums. In addition to these hemorrhages several bluish bruise-like subcutaneous hemorrhagic patches were observed during August and September, 1908. They were nearly all on the limbs. It is a question whether these various hemorrhages, as well as an urticarial tendency noted in February and March, 1908, might not be connected with diminished coagulability of the blood, or increased tendency to hemolysis (see later on).

Condition of the Blood. On May 19, 1908, the number of red cells in the cubic millimetre of blood had risen from 900,000 (on admission) to 2,000,000, and the hemoglobin from 18 per cent. to 35 per cent., but this improvement was hardly maintained. On July 4 the red cells were only 1,550,000, and the examination of blood films still showed the presence of typical megaloblasts. On August 15 another blood count was made. The red cells were then 1,300,000 and the white cells 8200 in the cubic millimetre. Dr. Boycott kindly forwarded the following differential count of 500 white cells: Lymphocytes, 51.2 per cent.; intermediates, 9.6; large hyalines, 1.2; neutrophile polymorphonuclears, 37.6; eosinophiles, 0.4; mast-cells, 0. He likewise reported that one neutrophile myelocyte and two nucleated red cells (small type with polychromatophilic cytoplasm) were found. The red cells showed moderate poikilocytosis and variation in size, but there were extremely few that were too big. The blood picture was certainly no longer that of pernicious anemia. By December 8 the number of red cells had risen to 3,277,000 in the cubic millimetre, and the hemoglobin was estimated by Haldane's method at 70 per cent.; nothing much abnormal could be made out by microscopic examination. On December 21 the red cells numbered 4,123,000, and the white cells 6250; hemoglobin, 74 per cent. Dr. Boycott, who again kindly examined blood films, found nothing abnormal in the red and white cells. His differential count of white cells then gave lymphocytes, 26.6 per cent.; intermediates, 2.2; large hyalines, 2; neutrophile polymorphonuclears, 68.4; eosinophiles, 0.8; mast-cells, 0.

It is interesting to note the increase in blood-viscosity accompanying the increase in the number of corpuscles. On February 23,

doubtless by reason of the corpuscular deficiency, the viscosity was very low; by Determann's clinical viscosimeter at 20° C. it was found to be only 2.6 times that of water at the same temperature. Estimated in the same way, on January 20, 1909, it was found to be 4 times that of water.

Owing to the hemorrhagic tendency manifested in the patient, her blood coagulability was repeatedly estimated by Sir A. E. Wright's coagulometer. The coagulation time varied on different occasions between ten minutes and fifteen minutes twelve seconds.

As it was supposed that excessive hemolysis might be the cause of the patient's acholuric jaundice ("acquired hemolytic jaundice" of A. Chauffard, F. Widal, Abrami, Brulé, etc.), the resistance of the red cells to hemolysis was repeatedly tested by Ribierre's method.[1] It was found that hemolysis usually occurred when a few drops of the patient's blood diluted with normal salt solution were added to a solution of between 0.46 and 0.44 parts per cent. of sodium chloride in distilled water. On one occasion it occurred still more readily (between 0.48 and 0.46), but lately the resistance of the red cells has apparently somewhat increased, for it now takes a solution of between 0.44 and 0.42 parts per cent. of sodium chloride in distilled water to produce hemolysis. The fragility, therefore, of the red cells, though rather high, appears not to be very greatly in excess of the normal. The hemolysis was not, however, examined by the method of adding the patient's red cells deprived of their plasma to the various solutions.

Dr. Leonard Dudgeon very kindly made some further investigations with the patient's blood on November 25, 1908, when her general condition was rapidly improving. From her blood he separated samples of her blood serum and of her red cells. He found that her serum had no hemolytic action on the red cells obtained from a normal (healthy) person or on her own red cells (that is, her serum possessed no autohemolytic action); neither did the blood serum from a normal person exert any hemolytic action on the patient's red cells. Furthermore, no hemagglutinative action was observed (by the methods employed by Dudgeon) on adding the patient's blood serum to a normal person's red cells, the patient's red cells to a normal person's serum, or the patient's serum to her own red cells.[2] No hemophagocytosis was observed.

On the whole, the present case seems to fit in best with the cases described by various authors on the Continent as examples of

[1] I am greatly indebted to Dr. Chapuis, one of the house physicians at the hospital, for much assistance in the clinical examination of the case, especially in regard to the hemolysis examinations, and to Dr. Trendelenburg, who replaced Dr. Chapuis for a short time.

[2] For Dr. Dudgeon's methods see his preliminary report "On the Presence of Hemagglutinins, Hemopsonins, and Hemolysins in the Blood Obtained from Infectious and Non-infectious Diseases in Man," Proceedings of the Royal Society, London, 1908, Series B, vol. lxxx, p. 531.

"Acquired Chronic Acholuric Jaundice with Splenomegaly and Anemia." The present case confirms Chauffard's opinion (as cited by Rolleston) that acquired cases of splenomegalic jaundice show more anemia and less jaundice than the congenital cases.[3] The remarkable feature of the case was the severity of the anemia which was at first accompanied by a myeloid (hemopoietic) reaction of the megaloblastic type, as in typical cases of pernicious anemia. It is not certain in the present case that the anemia was really hemolytic in origin, although the resistance of the patient's red blood cells to hemolysis was decidedly less than that noted in various healthy persons (controls) with whose blood hers was repeatedly compared.

Postmortem examinations have shown that some cases of acquired chronic acholuric jaundice are complicated by cholelithiasis. In the present case, indeed, the abdominal pains gave rise to a suspicion of gallstone trouble, while the recurrent attacks of epistaxis suggested the association of hepatic cirrhosis. The possibility of cholelithiasis secondary to chronic infection of the bile passages with typhoid bacilli was likewise considered, but the patient says she has never had typhoid fever, and her feces have been bacteriologically examined for typhoid bacilli with a negative result; moreover, Widal's reaction was twice tried, and on both occasions the result was negative.

The great improvement that has taken place in the patient's condition is very satisfactory, but this result cannot with certainty be attributed to the atoxyl treatment, as the period of the most decided improvement commenced a considerable time after the atoxyl treatment had been concluded. The main improvement appeared almost sudden enough to be termed a "crisis," but it was not accompanied by the blood changes (especially the large proportion of erythroblasts, some of them in stages of mitotic division) characteristic of typical "blood crises" in various forms of chronic anemia; that is to say, unless a true blood crisis of the kind commenced and ended during a specially long interval between two blood examinations.

[3] I have, however, satisfied myself that patients with congenital splenomegalic acholuric jaundice may sometimes (for a time at least) completely lose their icteric tinge. In other words, the jaundice may disappear and leave a condition of splenomegalic anemia only. Moreover, in the same family one child may suffer from congenital splenomegalic acholuric jaundice, whilst another child may suffer from chronic splenomegalic anemia without any manifest jaundice, though the blood picture be the same in both children. Evidently, in such instances the splenomegalic anemia is the same disease, whether it be accompanied by visible jaundice or not.

THE MEANS BY WHICH INFECTIOUS DISEASES ARE TRANSMITTED.

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The belief that infectious diseases are commonly transmitted through the medium of clothing, baggage, cargoes of vessels, rags, money, etc., constitutes what is known as the fomites theory. This has been so universally accepted that even the most reliable and satisfactory proof which may be presented in opposition to it, is reluctantly admitted. The fomites theory in some form has existed from the earliest times, and therefore it could not have been suggested as the result of careful scientific investigation. Since the publication of the bacteriological researches of Pasteur and Koch about 1880, practical sanitarians who have given this subject close and careful observation have been slowly but surely securing indisputable evidence that the material or articles above referred to transmit disease only in rare instances. The fomites theory is plausible, and also very popular, for when it is accepted as an explanation of an outbreak of infectious disease in a community, a thorough and extended inspection to detect the presence of other cases, which necessarily involves considerable time and trouble, is not urgently called for. Less than ten years ago a statement that yellow fever was not transmitted by fomites would have been promptly rejected, and would have found but few if any supporters, because the evidence presented as proof that clothing, etc., transmitted this disease was believed to be conclusive. We now know that yellow fever is transmitted only by the mosquito, and that clothing, bedding, and even the discharges of the patient do not act as a medium of infection and are perfectly harmless. It has also been proved that the mosquito is the only medium of infection in malaria; however, until recently the theory prevailed that this disease was transmitted by miasma, or poisonous emanations from swamps. Furthermore, it was believed that plague was commonly transmitted by fomites; now satisfactory proof has been presented to show that this disease is communicated by the rat, through the medium of the fleas which infest them, and that fomites have but little if anything to do with the extension of the disease. Thus are rejected theories regarding the transmission of infectious diseases, which have not been subjected to careful study, or supported by scientific and practical evidence.

While many are willing to change their views regarding the means by which yellow fever and some other diseases are transmitted, they still claim that clothing, rags, etc., constitute an active agent in the transmission of smallpox, typhus fever, measles, and

scarlet fever, although there is an abundance of reliable evidence to show that this is not true. I may cite an instance that occurred in my own experience, which presented an unusual opportunity to study this subject. During the fall of 1892, an outbreak of two of the most infectious diseases with which we have to deal, that is, smallpox and typhus fever, occurred in New York City and continued during the following spring (1893), involving 842 cases of smallpox and 714 cases of typhus fever, almost all of which were removed from tenement and lodging-house districts. The Bureau of Contagious Diseases of the Department of Health then consisted of about 80 persons, including diagnosticians, medical inspectors, disinfectors, ambulance drivers, etc., who were more or less constantly in close and prolonged contact with the cases in overcrowded and ill-ventilated apartments. These men wore no gowns and were protected in no other way. They went frequently and freely to and from their homes; but during the entire period not a case of smallpox or typhus fever was transmitted to members of their families or their friends. Such evidence as this deserves the most serious consideration and points to but one thing, that the clothing and effects, particularly of well persons, is a very uncommon means of transmitting disease. We find statements that smallpox infection is carried through the air to a distance of half a mile or more; that clothing which has been laid away for years may act as a medium of infection when exposed, and that persons have become infected in rooms which, months previously, had been carefully disinfected. Such statements as these, in view of the knowledge we now possess, are accepted by practical sanitarians with a great deal of skepticism. Coincidences are chiefly responsible for the apparent proof of these statements, and I have many times, by continued investigation, proved this to be the case. It is true that the specific organisms of typhus fever, measles, scarlet fever, and some infectious diseases have not yet been identified. Still we are justified from our knowledge of known specific organisms to decide approximately the power of resistance, etc., of the unknown ones; besides, we have no good reason to assume that in the diseases just referred to the specific organisms are any longer lived or resisting than those which have already been identified.

During the outbreak of smallpox and typhus fever in New York City in 1892–93, to which I have already referred, the most careful and painstaking investigation was made in connection with every case brought to the notice of the Board of Health. As a result satisfactory evidence was constantly being presented to show that these diseases were transmitted by personal contact, and not by the clothing and effects of well persons. I remember distinctly one instance in which it appeared that the fomites theory only could satisfactorily explain the appearance of a case of typhus fever, and the sequel showed what a careful investigation will usually prove.

A case of typhus fever occurred in the lower and east side of the city, which at first was not correctly diagnosticated or reported to the Department of Health. Among those who visited the patient was a married woman living in the upper part of the city on the west side. At the time of her visit she took with her a friend, a woman from Philadelphia. Her husband did not accompany her, nor did he at any time visit the case. About ten days after the visit the married woman was taken ill with typhus fever. A day or so subsequent to this the husband was also taken ill with typhus fever. This seemed to be reasonable evidence that the latter was infected through the medium of the clothing of his wife or her friend, who remained well. If the fomites theory had prevailed, this history would have constituted sufficient evidence as to the manner in which the disease was transmitted, further investigation would have been discontinued, and the case would have been referred to as satisfactory proof that clothing transmits disease. However, this view was not taken, and the names and addresses of the man's relatives and friends, and the places visited by him, were carefully obtained and a thorough investigation made. This showed that the husband was in the habit of spending a large part of his time in one of the low saloons on the extreme west side of the city, and had been a constant companion of a group of men in this place, two of whom had been removed some time previously to the hospital with typhus fever. Although the period of invasion of typhus fever is short and persons affected with this disease as a rule promptly succumb, there were cases during this outbreak removed from lodging houses, cheap saloons, etc., who had been sick for a day or so without the disease having been detected, or the patient seeking relief, and there is no reasonable doubt that the man referred to contracted the disease through this source, particularly as it is well known that typhus fever is more easily transmitted in close and badly ventilated apartments. This may illustrate one of the coincidences that not infrequently occurs; in the absence of a careful investigation it lends valuable support to the fomites theory, and, if accepted, discourages thorough investigation to discover the real cause of outbreaks of infectious disease, and in this way aids in their extension.

It is also a common belief that rags and money are usual agents in the transmission of disease, and it is also believed that certain infectious diseases, such as measles, scarlet fever, and diphtheria, are greatly increased at the opening of the school term, because infection is transmitted to others by the clothing of well children in whose families some form of infectious disease exists. Considerable literature is presented in support of these theories.

During the past few years municipal health officials, particularly those in the larger cities, have had ample opportunity to investigate the means by which infectious diseases are transmitted in schools.

School corps have been appointed, consisting of medical inspectors whose duties require them carefully and frequently to inspect each child in the public schools. The work has presented some rather astonishing and particularly satisfactory results; children are constantly being found in the schools apparently well, but who are in the active stage of infectious disease in a mild or unrecognized form, or are in the convalescent stage. In schools where the secretions from the throat and nose are subjected to a bacteriological examination, many children are found to have diphtheria bacilli, but without visible evidence of the disease; and what is believed to be an ordinary sore throat is frequently proved to be scarlet fever, with the accompanying desquamation. Besides children apparently affected with simple coryza are often found to have measles. These results are constantly being presented wherever this careful investigation is in operation, and offers a sane and practical explanation of the spread of infectious disease in these institutions.

The belief that rags used for commercial purposes, particularly those which are soiled, transmit disease is a favorite theory, and is apparently reasonable, as rags come from all parts of the world—frequently from areas where infectious diseases are known to exist. It is often reported, and alleged satisfactory evidence produced to show, that infectious diseases occur in paper warehouses as the result of this means of infection. I have given this part of the subject long and careful investigation, and have yet to find conclusive or satisfactory evidence that either domestic or foreign rags act as a medium of infection. In addition to my researches in this country, I personally investigated this subject in Egypt at the rag depots at Alexandria. Egyptian rags consist principally of the worn-out garments of the natives, which consist of one piece similar to an ordinary night-gown, and is usually worn directly against the skin. Therefore, as smallpox, or some other infectious disease, is almost always present in Egypt, it is fair to assume that the rags there would be a good test as to the possibility of this material acting as a means of infection. The carefully prepared statistics furnished me by the English sanitary authorities, who are in charge of this work in Egypt, showed not the slightest evidence that the men, women and children who were constantly in contact with these rags in the sorting room were more prone to infectious disease than those following other pursuits. It has been suggested by those who believe in the fomites theory, that probably foreign rags do not transmit disease because a long period occurs between their collection and the time that they are used in the manufacture of paper here. My investigation in Egypt related to domestic rags which had recently been collected, although when they reach this country they become foreign rags.

Paper money is also regarded as an ordinary medium of infection. Fortunately, in this instance, it is not very difficult to reach a scien-

tific and practical conclusion in regard to the danger from this source, as it is only necessary carefully to investigate the subject in connection with the employes of banks and other places where money is constantly being handled. Such an examination will show that these persons do not have infectious diseases any oftener than anyone else. The most effective test may be found in the statistics of the Treasury Department at Washington, in relation to which I have already conferred with the United States Treasurer. It will be shown that although many clerks are constantly handling and rehandling enormous quantities of old and filthy money, there is no proof that this article is a medium of infection. If an employee of a rag house or a bank becomes ill with an infectious disease, it is usually heralded as proof that these articles transmit infection: as a matter of fact, this is not scientific proof. In the consideration of this subject, it seems to be almost entirely forgotten that persons who work among rags or in banks are subject to the same outside exposure and danger of infection that others are, and the fact that they are ill with one of these diseases may be superficial, but not scientific, evidence that money or rags transmit disease. This would be indicated if proper proof were presented to show that those who handle rags or money contract infectious diseases oftener than others. Exhaustive investigation proves that this is not the case. If rags and money transmitted disease, the evidence of it would be forced upon us—we would not have to look for it.

In connection with this, I may add that a careful bacteriological investigation made by Mr. Warren W. Hilditch, at the Sheffield Laboratory of Bacteriology and Hygiene at Yale University, regarding paper money as a medium of infection,[1] goes a long way to confirm the statement which I have many times publicly made regarding this subject. Mr. Hilditch's article concludes as follows: "From the observation that I have made it would seem that the bacteria present on paper money are non-virulent, and that the form most present are the air forms. . . . One conclusion that may be drawn after a careful study of this subject is that money constitutes an unimportant factor in the transmission of disease. . . ."

Practically, it is only the plausibility of the fomites theory that supports the belief that cargoes of vessels transmit disease, because there is no satisfactory or reasonable proof of it. Fears are sometimes expressed that old rugs, etc., from the East and other sections where infectious diseases are more or less constantly present may act as a medium of infection. The danger of this exists almost entirely in the minds of those who present these theories. The diseases in the Orient which are to be feared are principally cholera and plague. Old rugs and curios are constantly being brought from that part of the world to New York—still these diseases do not appear as a result of the exposure of these articles.

[1] Popular Science Monthly, August, 1908.

At the New York Quarantine Station cargoes of vessels are not disturbed even when infectious diseases are found on board, and not the slightest evidence has been presented to show that this policy has in any way contributed to their extension. On the other hand, it relieves commerce of an enormous expense and great delay, which the treatment or disinfection of a vessel's cargo would involve. What has been said relative to cargoes of vessels may also be applied to baggage, etc.

Curiously enough, the concern with which some regard clothing, rags, etc., as a means of infection does not extend to a consideration of the real danger of discharges from the respiratory and alimentary tract of persons ill with certain infectious diseases. No one doubts that the stools of typhoid fever patients transmit this disease; still, they are carelessly handled in the sick room. The means which are usually taken to render them harmless consist in the addition of a liquid disinfectant which may or may not be left for a short time in contact with the mass, the mixture afterward being thrown into the water-closet or privy vault. Discharges from the respiratory tract are often treated in practically the same way. Experiments made at the New York Quarantine Laboratory show that disinfecting solutions, such as chloride of lime, carbolic acid, etc., do not disinfect when used in the manner above described. The experiments consisted in treating fecal matter in receptacles with the agents above referred to. It was found that at the end of twenty-four hours only the most superficial part of the mass was affected. Similar experiments conducted by Dr. William H. Park, of the Department of Health of the City of New York, produced practically the same result. This would indicate clearly enough that dis infecting solutions added to discharges are of no value unless they are thoroughly incorporated with every portion of the mass to an extent which would be hardly practical to carry out, and I am quite sure that no nurse or other attendant upon the sick would take the time to do it. Therefore, infected stools under the ordinary treatment are not disinfected, and remain a medium of infection. Discharges from the respiratory tract are also frequently dropped into receptacles containing disinfecting solutions or powders, for the purpose of destroying the specific organism which they contain. As mucus is particularly tenacious and resisting, it is very doubtful if the disinfectant, with which this comes in contact, ever properly fulfils the requirement.

It is generally believed that privy vaults may be disinfected by the use of various solutions and powders: such a thing is practically impossible. If a single discharge cannot be disinfected by lime, carbolic acid, etc., certainly a receptacle containing a large amount of fecal matter in all stages of consistence and decomposition cannot be. In small communities which have no sewerage system, it is required that each house shall have a receptacle for the deposit of

fecal matter. In the presence of typhoid fever, for instance, the proximity of these receptacles or privy vaults to wells (which are commonly near by) is very properly regarded as not an uncommon means by which infection is transmitted. So far as the ordinary privy vault is concerned, there is not the slightest reason or justification for its existence. If a receptacle of this kind is necessary it should be placed above the ground, and not below it. This method of construction answers the requirement, and insures an air space underneath, which practically prevents ground contamination and the transmission of infection even when only ordinary care is observed, and renders any attempt at disinfection practically unnecessary.

It is evident from a careful review of this subject that there is not a uniformity of opinion regarding the usual means by which infectious diseases are transmitted. The bar to this has unquestionably been the popularity of the fomites theory, not because it has been supported by scientific evidence, but because it presents a prompt and easy explanation for outbreaks of infectious disease; besides, there are many who believe we should discard no theory which may possibly aid in the prevention of infectious disease, whether or not it is reasonable or scientific.

No one who has had long practical experience with infectious disease doubts that in some unusual and rare instances clothing, rags, or almost any article may transmit disease. However, this is not the most important factor for practical sanitarians to consider. In order to deal successfully with outbreaks of infectious disease, we must ascertain what are the usual or ordinary means by which they are transmitted, as these must decide the character of regulations to be enforced and the precautions which must be taken to prevent their extension. General regulations cannot be made to deal with rare exceptions. If an attempt is made to do this, both the public and commerce are unfairly and unjustly treated, and unnecessary annoyance, delay, and expense is involved. Modern practical sanitation does not insure complete or absolute safety in its operation, and efforts made to secure this almost always defeat the end in view.

The acceptance of the fomites theory as an ordinary medium of infection aids in the extension of infectious disease, chiefly because public health officials who believe in this cannot fully appreciate the imperative necessity for an extended and thorough inspection to detect the presence of other cases, which are usually responsible for the extension of infectious disease. What I have said in regard to this subject is not intended to imply that we should dismiss entirely from our minds the possibility or probability of fomites transmitting disease. The clothing, bedding, etc., in contact with persons actively sick, which sometimes contain discharges, etc., if exposed to other persons within a comparatively short period may

transmit disease, and it is for this reason that the disinfection of the contents of the apartment of the patient is justified. As I have already stated, in rare or unusual instances, the clothing or effects of well persons may be the medium of infection; however, this happens so seldom that it is only entitled to secondary consideration.

Indisputable evidence has been presented to show that infectious diseases are usually transmitted directly from the sick to the well. Besides, in recent years we have learned of another common means by which infectious diseases are transmitted, of which conclusive proof has been presented, and that is that well persons act as carriers of pathogenic organisms without presenting constitutional or local evidence of it. This refers to the diphtheria and typhoid organisms, and particularly to the cholera bacilli. There is no doubt whatever that cholera is frequently spread by well persons in whose alimentary tract the germ of cholera is present, and who are responsible for outbreaks of this disease by infecting in various ways food and drink without exhibiting any symptoms of the disease themselves. Then we have the transmission of disease by insects. With such known means of infection as these we are hardly justified in considering clothing, etc., as usual agents of infection, particularly as these articles can hardly be regarded as a proper media for organisms even for a brief period; besides, organisms which usually cause infectious diseases in human beings contain no spores.

There can be no question that the secret of success in dealing with outbreaks of infectious disease consists in the most thorough and extended inspection and investigation to discover the presence of the sick, and, when found, to secure their prompt and careful isolation. This is applicable to tuberculosis also, and there is no doubt that the proper and logical means of exterminating or controlling this disease is by isolation. In addition, we must always bear in mind the probability of infection being transmitted by well persons or carriers, and also insects. These constitute the modern and scientific methods of treating these emergencies. If they are employed, there will be no outbreak which cannot be brought under control, and the ravages which infectious diseases have caused in the past, and which are even now occurring in certain sections of the East, need never occur again. The fomites theory is not in harmony with these principles, neither can those who support this theory fully understand the frequency with which outbreaks of infectious diseases are caused by mild, ambulant, or unrecognized cases, which I believe constitute one of the most common and dangerous factors with which we have to deal. In my experience, both in municipal work and at Quarantine, abundant evidence of this is constantly being presented, and, furthermore, that this type of disease can be detected only by a most careful inspection; for instance, two of the cases of bubonic plague which were discovered on incoming vessels at the New York

Quarantine during the past few years were so mild that the men affected were not confined to their quarters, but were able to perform at least part of their work, and would have passed an ordinary visual examination. It was not until their temperatures were taken, and a careful glandular examination made, that the disease was identified. Very mild cases of smallpox, yellow fever, etc., are not uncommonly found on incoming vessels, chiefly because they are looked for. If these cases were not detected on shipboard and were allowed to proceed to their destination and there cause secondary cases of these diseases, the fomites theory would unquestionably be called upon to explain the outbreak. The value of a careful inspection and investigation in the presence of infectious disease is not only of great importance at the point where the outbreak occurs, but frequently aids in the detection of similar cases among the patient's family or friends who may recently have been with him, and who are residents of other towns. This extended investigation is frequently most fruitful in its results.

The knowledge we now possess regarding the means by which infectious diseases are transmitted, justifies a great diminution in the disinfection hitherto performed. The disinfection of the clothing, baggage, etc., of well persons who have been exposed to the sick, or have been in infected areas, the cargoes of vessels, rags, money, etc., should be eliminated from this treatment unless there is some specific reason for employing it. The cargo of a vessel cannot be disinfected unless it is removed from the ship, notwithstanding statements to the contrary. This is an exceedingly expensive process and involves great delay and annoyance to all concerned, and I have yet to meet with an instance where it was justified. Gaseous disinfectants cannot be depended upon to penetrate, and are of value only when the material to be treated is fully exposed or spread out. Therefore, the introduction of sulphur dioxide, or formaldehyde, into the hold of a vessel for the purpose of disinfection would practically be valueless. As rags for commercial use usually consist of small pieces, which could not be properly spread out, it would be necessary to disinfect them in bulk by steam. This process would be exceedingly expensive, particularly if applied to imported rags which arrive in tightly rolled bales. Although steam has great penetrating power, it could not be depended upon to enter sufficiently far into these packages to insure a germicidal action, and the packages would have to be opened for treatment at the port of destination, as it would probably never be done at the point of collection, or at the port of embarkation. The question of the disinfection of money can be dismissed in a word—any attempt to carry this out would be farcial and of no practical value.

The requirement of the fomites theory frequently involves the detention at home of those who have been exposed to infection, or in whose home infectious disease may exist, for the reason that the

clothing of these people is believed to transmit disease. In many instances this is a great hardship, and frequently seriously interferes with the family revenue. The modern view of this subject does not justify this procedure, particularly when the patient is properly isolated and cared for. In these instances it is only required that a daily examination shall be made of suspects, which should include the use of the thermometer to early detect the invasion of disease.

Unnecessary disinfection has led to a misunderstanding of its function and value. It is frequently left for members of the family or other laymen to carry out, whereas, when it is required, its application should be under the immediate direction of the physician or health official in charge, and should be performed in a proper and scientific way. We still find saucers of carbolic acid, etc., placed under the bed and about the sick room, and it is not uncommon to find that small pieces of sulphur are occasionally burned in the room for the purpose of disinfecting it. It is hardly necessary to say that these attempts to disinfect an apartment are perfectly worthless, and only annoy the patient and belittle disinfection.

I have already referred to the inefficient methods which are used at present, both in hospitals and dwelling houses, in the treatment of the discharges of those who have infectious disease, which I am sure all agree constitutes a very important means of infection. From a practical standpoint there is but one agent that can be depended upon to destroy the organism in this matter, and that is heat, either by boiling or incineration. The principle of modern sanitation, which governs this detail, requires that discharges, refuse, etc., shall be destroyed as near as possible to the point of production, and heat is the proper agent for the purpose.

Boiling water is one of the most valuable and practical disinfectant we possess, but unfortunately it is not fully appreciated. Its action is sure, it is safe, simple, and without expense. The destruction of the specific organism in the discharges of the sick by boiling water is under ordinary circumstances an easier and a more practical method than incineration. At present, a simple boiler is successfully used at the Swinburne Island Hospital, New York Quarantine, for this purpose. Its action is quick and made practically odorless by having a close fitting cover, from the top of which an outlet connected with a flexible tube conducts the steam outside of the window. An apparatus suitable for this purpose can be made by any tinsmith for a small price, or if necessary can be improvised by the use of ordinary household appliances. In the country this method would practically prevent danger from infection through the medium of a privy vault.

The practical abandonment of the fomites theory not only does not, as many believe, involve danger, but substitutes for it a scientific, practical, and successful means of dealing with outbreaks of infectious diseases.

UNCINARIASIS IN PANAMA.

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It is not the object of this paper to discuss the general pathological anatomy of fatal cases of uncinariasis, but rather to note the presence of hook-worms in the routine autopsy cases, and the fact that the old world hook-worm (Ankylostomum duodenale) and the new world hook-worm (Necator americanus or Uncinaria americana) are often present in the same case. A few points relating to the pathology of the jejunum will be discussed—especially hemorrhage and inflammation in the submucosa. No attempt will be made to review the literature which has been very carefully compiled by A. Looss.[1]

During the year from September, 1907, to September, 1908, 420 autopsies were performed at the pathological laboratory of the Ancon Hospital, C. Z., Panama, and in the last 232 cases the intestinal parasites were studied with some care. In this series of 232 consecutive cases the presence of hook-worms was recorded in 72 cases (31 per cent.). In 39 cases no mention of intestinal parasites was made, but we feel sure that in these cases the hook-worm was absent. If, however, this number is deducted from 232, the percentage of cases infected with hook-worms rises to 37 per cent. The whites in this series numbered 37, with but 2 cases of uncinariasis, a frequency of only 6 per cent. Both cases were in Spaniards. The whites included Americans, Spaniards, Greeks, Italians, etc. The blacks came principally from the Southern West Indies and Central America. If we deduct the white cases, we find the frequency of hook-worm infection to be 36 per cent. Heavy infections with hook-worms were not common, and cases showing 100 or more worms occurred only five times in the 232 cases. Both old and new world varieties were present in every one of the severe infections, Necator americanus predominating. Of the entire 420 cases, only 9 showed a heavy infection—that is, over 100 worms. These cases came from Jamaica (3), Martinique (2), Costa Rica (1), Colombia (1), Antigua (1), and Guadeloupe (1). As the sanitary conditions on the canal zone are excellent and most of the laborers wear shoes, we may say that the great majority of these cases were infected in their native lands. The length of their stay on the Isthmus varies from one month to two years. Cases among native Panama negroes show light infections, but both types of the hook-worm are present.

The old world hook-worm (Ankylostomum duodenale or Uncinaria duodenalis) was present in 39 cases (17 per cent.), and in 25 cases was found associated with the new world variety (Necator ameri-

[1] Handbuch der Tropenkrankheiten, 1905, i, 116; Centralbl. f. Bact., 1907, xxxv, 752.

canus). The new world hook-worm was present in 49 cases (21 per cent.), and predominated in all heavy infections.

It is not a difficult matter to separate the two types of hook-worm. The parasites were washed in running water until clean, then placed in Petri dishes on a glass plate painted black. After some practice, one can separate the two types by using the lens of a dissecting microscope. The old world worm is thicker, and has a milky look. It is more active, and has a blunt head end. The mouth and œsophagus are over twice the size of those of the new world variety. The new world worm has a more delicate body, with a smaller head end and œsophagus. It has a more translucent appearance, except when containing blood. The two types of worms separated with the aid of a low-power lens are placed in saline solution in rows on slides and examined under a No. 3 objective (Leitz). The four prominent hooks found in the mouth of the old world worm are easily seen, and establish the diagnosis. In many cases the dorsal rays of the caudal bursa in the males were studied, as well as the location of the vagina in the females. Ankylostomum duodenale in appearance corresponds very closely with Ankylostomum caninum, which is present in great numbers in all the native dogs.

232 CASES: 37 WHITES; 195 BLACKS.

	White.	Black.	All Cases.
Hook-worms present	2 cases (6%)	70 cases (36%)	72 cases (31%)
Old world hook-worm, Ankylostomum duodenale	2 cases (6%)	37 cases (19%)	39 cases (17%)
New world hook-worm, Necator americanus	2 cases (6%)	47 cases (24%)	49 cases (21%)
New and old world hook-worm together in same case	2 cases (6%)	23 cases (12%)	25 cases (11%)
Whip-worm (Trichuris triciura)	3 cases (8%)	37 cases (19%)	40 cases (17%)
Ascaris lumbricoides	(0%)	19 cases (10%)	19 cases (8%)

The following table comprises 62 cases, in which the worms were studied and classified. In some cases the males and females were not separated and numbered, but this was carefully done in the majority of cases. The intestinal tract opened, but not washed, was looked over by a labaratory assistant, who picked out most of the worms; then the person performing the autopsy examined it carefully and collected any remaining parasites. We feel sure that very few worms escaped this routine examination. Whip-worms and round-worms were recorded in the 232 cases. Whip-worms were present in 40 cases (17 per cent.)—three of the cases were in white patients. Ascaris infection was found in but 19 cases (8 per cent.), all in black patients; 134 cases were free from intestinal parasites (58 per cent.).

Home.	Uncinaria.				Whip-worm.	Ascaris.	Remarks.
	Americana.		Duodenalis.				
	F.	M.	F.	M.			
Jamaica	91	43	17	4			Worms contain fresh blood.
Jamaica	60	26	3	1			Worms contain fresh blood; many submucous ecchymoses.
Jamaica	2	2	16	22			Worms contain fresh blood.
Jamaica	(20)						
Jamaica	2	1			1		
Jamaica	2	4					
Jamaica	4	2					
Jamaica	1				2	1	
Jamaica			(3)				
Jamaica	(8)						
Jamaica		1				1	
Jamaica	+		+		+		
Barbadoes	14	5	3	2	3		Many submucous hematomas.
Barbadoes	8	2	1		1		
Barbadoes	2	2	6				
Barbadoes	2	1			1		
Barbadoes	(5)						
Barbadoes			2	4	1		
Barbadoes			2	2			
Barbadoes	3						
Barbadoes			1				Many submucous hematomas.
Barbadoes			1			2	
Barbadoes	(1)						
Barbadoes			1				
Barbadoes	Few hook-worms.						Many submucous hematomas; blood cyst contains hook-worm.
Barbadoes			+				
Martinique	(200)		3	4			Worms contain fresh blood.
Martinique	82	77	9	8	1		Many submucous ecchymoses, worms contain fresh blood; small blood clots adherent to mucosa.
Martinique	9	6	4		1		Worms contain fresh blood.
Martinique	10	4			6		
Martinique	3		15	4	1		
Martinique	3	1			9		
Martinique			2				
Martinique	(1)		(1)				
Martinique	+		+				Many submucous hematomas; blood cyst contains hook-worm.
Antigua	(100)		(60)				
Antigua	2		(30)				
Antigua			1	1			
Grenada	(38)		(1)				
Grenada	(35)		(2)				
Grenada			1				
Gaudeloupe	(11)		1	1	2		
Gaudeloupe	(6)				1		Many submucous hematomas; blood cyst contains hook-worm.
Trinidad	19	9	25	30			Many submucous ecchymoses;
St. Vincent	6	5			1	2	many submucous hematomas;
St. Lucia	(1)				1		small blood clots adherent to mucosa.
. . .	6	3					Many submucous hematomas;
Spain	(20)		(3)				blood cyst contains hook-worm.
Spain	2	2	3		3		
Cuba	2						
Panama	(75)						
Panama	(10)		(2)		12	1	
Panama	11	3	1	1	1		Worms contain fresh blood.
Panama	8	2				12	
Panama			2	1	4		
Panama				1			
Colombia	23	19			3		
Colombia	8	7	1				
Colombia			(2)			3	
Colombia	1						
Costa Rica	1		1				Worms contain fresh blood; many submucous hematomas.
Costa Rica	(100)		(10)		3		Many submucous ecchymoses; worms contain fresh blood.

A glance at the table under "Remarks" will show that our findings do not correspond with those of Ashford and King,[2] in Porto Rico, concerning intestinal ecchymoses and the presence of blood in the digestive tract of the hook-worms. They state that ecchymoses are very rare, only a few being found in a single case in their series, and that the worms very rarely contain blood.

Ecchymoses in the mucosa or submucosa were a common finding in the jejunum infected with hook-worms, both at the point of attachment of the worm's head and in other places where presumably the worm had been feeding. When the area of hemorrhage exceeded 3 to 4 mm. in diameter, it was referred to as a "submucous hematoma." A note of "ecchymoses" or "submucous hematomas" was made in 18 cases, and in several cases they were very numerous (No. 1441), giving a speckled appearance to the mucosa.

The blood cysts described by Bilharz and Grassi were not infrequent, and were often found with an included hook-worm—7 cases (Figs. 1 and 2). Such cysts measured from 5 to 10 mm. in diameter; more rarely the worm was completely buried in the submucosa with very little extravasation of blood (Fig. 2). Sections show great numbers of large intestinal bacilli associated with the worms buried in the submucosa, and these bacteria cause an extensive inflammation of the adjacent mucosa and submucosa which are infiltrated with large numbers of polymorphonuclear leukocytes and eosinophiles.

This series of cases shows that the worms often contain fresh blood, both the new and old world forms, more frequently the latter. A note that "many worms contain fresh blood" was made in 16 cases, and it was unusual not to find a few worms containing blood in an infected case when the autopsy was performed within two or three hours after death. It was noted that in cases of advanced anemia the worms rarely contained blood, while in cases showing no anemia the worms very often contained fresh blood and ecchymoses were more evident. This may explain the findings of Ashford and King, who maintain that the hook-worms very rarely contain blood. These writers examined fatal cases of uncinariasis which showed extreme anemia. When worms which were full of bright blood were removed from the intestinal mucosa and placed in water or 0.8 per cent. saline solution, they soon discharged the blood. Under the microscope one could watch the red blood cells and blood-stained fluid being poured out from the mouth and anus. This explains the fact that worms found in the feces or at an autopsy performed several hours after death may contain very little or no fresh blood.

Looss and others insist that the worms live on the intestinal epithelium, and cannot digest the blood. It seems rather hasty to

[2] Jour. Amer. Med. Assoc., 1907, xlix, 471; Boston Med. and Surg. Jour., 1907, clvi, 415; Report of the Commission for the Study and Treatment of Anemia in Porto Rico.

decide that a worm can digest epithelial cells from the human host, yet cannot digest red blood cells.

FIG. 1.—Blood cyst below the mucosa of the jejunum, with cross-section (a) of included hook-worm.

FIG. 2.—Hook-worm in the submucosa, with very little extravasation of blood; cross-section of the body of a female worm.

The following fact proves that the hook-worm can live and thrive for a considerable length of time in blood. Hook-worms removed from the "blood cysts" in the intestinal mucosa were invariably very active and vigorous and contained fresh blood. Sections through some of these "cysts" showed an invasion of the blood and adjacent submucosa by leukocytes and various wandering cells in considerable numbers. Such a reaction required from two to four days, during which time the worm lived in the blood and ingested more or less of it, as can be seen in sections which show the

FIG. 3.—Jejunum in a fatal case of uncinariasis, showing extensive scarring and inflammation of the intestine. (*a*) Bases of crypts of Lieberkühn; many polymorphonuclear leukocytes in the interglandular tissue; (*b*) muscularis mucosæ distorted and scarred, invaded by many wandering cells, many of them eosinophiles; (*c*) submucosa, which is much thickened and full of every type of cell—eosinophiles, polymorphonuclears, and "polyblasts." There is much scar tissue; new-formed bloodvessels are seen.

worm's intestine to contain red cells and granular detritus. It is admitted by all writers that blood is found in the worm's intestine, and it seems reasonable to conclude that the parasites live on both the blood and the epithelium, but we feel sure that the blood is the main factor when the worms are feeding on a fairly normal mucosa. In a heavily infected case, when the mucosa is very anemic, somewhat thickened, and infiltrated with leukocytes (Fig. 3), it is fair to suppose that the worms may live chiefly on the epithelium and mucus. Sections of worms show the intestinal canal containing red blood cells, coagulated albuminous detritus, and epithelial cells.

Many writers (Ashford, Baker,[3] Yates[4]) believe that uncinaria produces some obscure hemolytic toxin analogous to that of Bothriocephalus latus, but this has never been demonstrated. Clinically, too, the blood pictures are very different (Boycott,[5] Adami[6]), as the anemia of uncinariasis is distinctly of the secondary type. I hope to show in another article[7] that the hook-worm of man does contain a hemolytic factor which is constant but very weak. It is present in all parts of the worm, probably in the intestinal canal—not in the cephalic glands alone.

That the hook-worm does not contain a powerful hemolysin is shown by a study of the "blood cysts" described above (Fig. 1). The worms often remain in these sumbucous blood clots for a few days at least, as shown by the number and type of wandering cells in the edge of the clot. The worms are not injured by their stay in the blood, yet there are well-preserved red blood cells in all parts of the "blood cysts." It seems that this is almost a perfect experiment performed by the hook-worm: the parasite is included in a small sac of the host's blood, and all conditions are as they should be to demonstrate the presence of a hemolytic agent—yet the blood cells are not dissolved in any great number. Here we have a small amount of blood isolated in the human tissues and containing an active hook-worm. In many cases there is less than 0.5 c.c. of blood in the cyst, and the parasite lives in this medium one, two, or three days, yet can cause no marked hemolysis. The parasite by its activity has deprived its host of a fraction of a cubic centimeter of blood, but cannot hemolyze this small amount during a considerable interval of time. Thus, the worm can cause the loss of more blood through damage to the mucosa than it can hemolyze under favorable conditions. It does not seem likely, therefore, that this same worm could secrete a hemolytic substance which, taken up by the human intestine, could act on the circulating blood, where surely conditions would be less favorable for hemolysis than in the "blood cysts." I believe that this observation alone is sufficient to exclude the presence of a powerful hemolysin in the hook-worm—a hemolysin which could be absorbed by the host and cause an advanced secondary anemia.

The cause of the anemia is not clear: various explanations have been advanced. Some writers disregard the blood abstracted by the worm, and the numerous "bites" which often bleed after the worm has changed its feeding ground (No. 1441). Loeb[8] has demonstrated a substance, which definitely inhibits the blood coagulation, to be present in the cephalic glands of Ankylostomum caninum, and this may be a factor in promoting the oozing of blood from the

[3] Brit. Med. Jour., 1903, i, 718.
[4] Johns Hopkins Hosp. Bull., 1901, xii, 364.
[5] Brit. Med. Jour., 1907, ii, 1318; Jour. Hyg., January, 1904, iv, No. 1.
[6] Montreal Med. Jour., 1903, xxxii, 186.
[7] Jour. Exp. Med., 1909, xi, No. 2.
[8] Proc. Path. Soc., Philadelphia, June, 1904; Centralbl. f. Bact., 1906, xl, 740.

mucosa. It has been proved that this worm is a bloodsucker, and the daily abstraction of a small amount of blood cannot be disregarded. Many writers attribute the anemia to an obscure toxin produced by the cephalic glands of the worm and absorbed by the host. No proof of the existence of any such toxin has been furnished, and until this proof is forthcoming such an explanation is merely evading the question.

Others (Ferguson)[9] have advanced the theory that the "bites," which are always greater in number than the parasites, cause little foci of infection in the mucosa, a chronic inflammation, and anemia. The anemia may be due to the poisonous products absorbed from these foci of inflammation in the intestine. This, I believe, is the most important factor in the production of the anemia, and explains the fact that some cases with relatively few uncinariæ may show a profound or even fatal anemia. Case 1137 may be cited as an example of this: A male, Jamaican, negro, aged sixty years, shortly before his death, had 15 per cent. of hemoglobin. There was nothing unusual about the gross pathology of the viscera. The tissues were all very pale. The heart was greatly dilated, with watery, pale clots—hydremia. The lungs were pale and cushiony. The liver and kidneys showed a definite yellowish brown pigmentation and anemia. The bone marrow was very firm, pink, and cellular. The jejunum contained between 100 and 200 hook-worms, but the types were not identified. The mucosa was very pale and smooth. There were no notes concerning the presence of fresh blood in the worms, and no notes regarding ecchymoses. We cannot assume that the worms were discouraged by the anemia, abandoned the mucosa, and were carried out in the feces, for we find cases with even greater anemia and many hundreds of worm in the intestines. Microscopic sections of this jejunum are most interesting (Fig. 3). The mucosa shows rather short villi and crypts, with a little distortion of the architecture of the glands, due to an increase in connective tissue. The interglandular tissue in the villi and at the base of the gland tubules shows a marked infiltration with polymorphonuclear leukocytes and eosinophiles, which in some fields are more numerous than the mononuclears. The muscularis mucosæ is thickened, scarred, and infiltrated with wandering cells of all types. The submucosa is thickened and scarred. It is not sharply separated from the muscularis mucosæ, and many polymorphonuclear leukocytes and eosinophiles are present. Accumulations of large mononuclear wandering cells are found about the vessels in the submucosa. The outer muscle coats are normal. This is a very definite pathological change, a picture of diffuse inflammation, evidently of some duration, due to the hook-worm, as evidenced by the eosinophiles.

When one considers the amount of tissue which was involved in this

[9] Brit. Med. Jour., 1907, ii, 1320.

change—several feet of the jejunal mucosa—it is not difficult to account for an advanced anemia. Perhaps the same explanation may hold for the liver necroses which were present in this case, and similar to those described by Yates in a fatal case of infection with the new world hook-worm. Many of the liver lobules show a necrosis of the central half or third, where the liver cells are quite hyaline, and wandering cells are invading such areas. The other liver cells show some fatty infiltration, and a deposit of a finely granular, yellow pigment.

Reasoning from this series of cases, it seems probable that the anemia of uncinariasis is due to two factors at least: (1) Loss of blood through feeding of the worms and oozing from damaged areas where the worms have broken the mucosa; and (2) infection of the intestinal mucosa and submucosa, due to bites of the worms which give points of entrance for intestinal bacteria.

SUMMARY. 1. Hook-worms are found in the routine autopsy examinations in 31 per cent. of the cases.

2. The old world hook-worm (Ankylostomum duodenale) is present in 17 per cent. of the cases, together with Necator americanus in 11 per cent. of the cases.

3. The new world hook-worm (Necator americanus) is present in 21 per cent. of all the cases, and predominates in all heavy infections.

4. The whip-worm (Trichuris triciura) is present in 17 per cent., and Ascaris lumbricoides in 8 per cent. of the cases.

5. Hook-worms removed from the intestinal mucosa a few hours after the death of a patient very often contain fresh blood.

6. Ecchymoses and small submucous hematomas are not rare findings in an infected jejunum.

7. Hook-worms ingest both blood and epithelial cells and presumably digest both.

8. The anemia is due not only to direct loss of blood through activity of the hook-worms, but to a diffuse inflammation of the mucosa and submucosa of the jejunum. This inflammation is caused by the bites of the parasites which damage the mucosa and give entrance to the intestinal bacteria.

9. The severity of the anemia depends upon the number of hook-worms, and upon the intensity and extent of this diffuse inflammation. This second factor may explain the cases of fatal anemia in which only relatively few hook-worms are present.

10. Study of the "blood cysts" containing hook-worms shows that the parasites can live in blood for days and cause no active hemolysis of this blood—strong evidence against the presence of a powerful hemolysin in the hook-worm.

In conclusion, it is a pleasure to express my sincere thanks to Colonel W. C. Gorgas and Dr. S. T. Darling, for permission to use the material at the Ancon Laboratory, and to Dr. A. H. Dodge, who assisted in much of the routine work.

MALIGNANT NEWGROWTH IN CHILDHOOD.

I. MALIGNANT DISEASE OF THE UTERUS, OVARY, AND VAGINA IN CHILDREN.[1]

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Reviewing the literature of malignant newgrowths in children one is struck with the increasing frequency with which diseases of the genital organs in children are being recorded. About twenty years ago, when I commenced to call attention to malignant diseases of the pelvic organs in female children, the references to be found in the literature were few indeed. I now make a special plea for the early recognition of malignant diseases in children. These diseases are no longer medical curiosities, but will be seen by all of us if they are looked for with care and intelligence. It is the early recognition that they need, because with early recognition early radical treatment will reduce the present rather apalling mortality. I make this appeal to the general practitioner; it is to him that we must look for any advances in our knowledge and treatment of these diseases. He has the first chance, and upon his diagnostic skill and acumen depends our ability to classify, study, and successfully treat the little sufferers.

Anyone who is specially engaged in the study of pediatrics will agree with the statement that female children, even young infants, are subject to the same affections of the genital organs that are found in adult females; in fact, they are probably more prone to at least one of them, notably gonorrhœa. We must also remember that many diseased states brought to our attention by adult women have their etiology in conditions which existed long before puberty was established. We rarely discover malformations of the genital tract in children, but they are studied with great ease in the adult. Salpingitis and localized peritonitis are rather frequent in little girls. Marx[2] reports the postmortem examination of fifteen children who had symptoms of salpingo-oöphoritis similar to those found in the adult. In five of them the Fallopian tubes contained pus and their uterine attachments were sealed.

The examination of a child, no matter how young it may be, for the detection of malignant disease, is in all respects similar to that of the adult, except the vaginal and bimanual examination. We rarely examine young children by the vagina; in fact, it is hardly

[1] Read by invitation at a meeting of the California Academy of Medicine, San Francisco, October 22, 1908.

[2] Gaz. de gynec., November 15, 1895.

justifiable, unless the disease is manifestly vaginal or a vaginal discharge is evident. When it is necessary to examine the vagina of a young child, the cystoscope of Kelly, No. 8, 9, or 10, as suggested by himself, will be found the most available instrument. It is introduced with great ease and little pain if cocaine has been used; the child soon gets used to it, and if necessary applications of remedial drugs may be made to the different areas. The knee-chest position is of great value in making these examinations; of course, the usual dorsal position is of great value, but in children it is less valuable than in the adult. Of greatest value of all in children is the rectal examination; a combined rectal and bimanual examination is ideal, no matter how young the child may be. If this be made a matter of routine, we shall be surprised how often grave disease is detected in these little bodies. Some years ago Carpenter, of London, was the anesthetizer for an examination of a case in obstinate constipation in a little girl which had resisted all usual methods of treatment. The examination was carried out by means of the rectal and abdominal method and a myeloid sarcoma growing from the anterior surface of the sacrum was found to be the cause of the obstinate constipation.

In young children, from birth to the fifth year, the relatively greater length of the examining finger in comparison with the small pelvis and small abdominal cavity permits wide excursions over practically all of the pelvis and almost the entire abdomen. Of course as the child grows older this examination is of less value, because the size of the body now nearly approaches that of the adult. The rectal examination is best made under an anesthetic; this may not always be necessary, but a gynecological examination in a resisting child is devoid of value. The child is placed in the dorsal position, the legs are flexed on the thighs and the thighs on the abdomen. The pelvis is elevated as for a cystoscopic examination. The examiner now places the left hand on the abdomen and the right index finger in the rectum. A routine examination is now made first of the left side of the pelvis and abdominal cavity and then to the right up to or above the level of the umbilicus, which can usually be reached with great ease. Any abnormal growth not only in the sexual organs and abdominal viscera, but in the intestines and retroperitoneal structures, may be readily recognized.

In little children the finger in the rectum and the hand on the abdominal wall are separated only by the thickness of the comparatively thin walls of the child's abdomen, and a growth can be outlined with startling exactness. The iliac, hypogastric, and umbilical regions are within one's grasp; the important regions of the appendix and the contiguous structures are almost within one's hand, and we can at once recognize the so-called intestinal matting; even a slight degree of peritonitis, just sufficient to agglutinate the omentum, may be recognized by the combined examination in expe-

rienced hands, particularly those hands that have learned to know that when peritonitis is present the intestines move en masse, as it were, and do not quickly glide under the fingers as the healthy gut will.

A note of warning must be sounded here in regard to the danger of mistaking a partially filled bladder for a tumor or a peritoneal exudation. The means of guarding against this error is self-evident; I only mention it because those of us who are teaching sometimes see the younger practitioner fall into error. We must also guard against mistaking a pus collection or serous accumulation for a filled bladder.

Let us for a moment consider the anatomical peculiarities of the female pelvic organs in children. The sacrum and in consequence the rectum are almost straight. One will miss the well-known hollow of the sacrum, and the large lax ampullar distention does not exist. In young children, those who have not walked much, the bladder is about the size and shape of an egg, the base downward, and its site is almost purely abdominal. As the child walks more the bladder sinks lower in the pelvis, but until about puberty it can readily be displaced into the abdominal cavity by an examining finger, so loose is its attachment. The infantile uterus has but little body; it is practically a thin cord made up mostly of the cervix which at first appears unduly bulky. It lies comparatively high in the pelvis, but can be rolled between the fingers and the symphysis pubis. In young children the ovaries are at the side of the pelvis close to the external iliac artery: the pulsation of this vessel is one of the guides for their location, the other being the sickle-shaped uterosacral ligaments. It is to be understood that these landmarks are subject to as many variations in the child as in the adult. The usual variation is a higher location, but we must remember those cases of congenital prolapse of the uterus to which I have called attention,[3] and we must distinguish this prolapse from congenital hypertrophic elongation of the cervix. The prolapse may be of any degree, and is usually without marked symptoms; indeed, some of the children have performed the functions of the bladder and rectum in a normal manner. These cases of congenital prolapse are likely to be associated with lumbosacral spina bifida and rectal ectropion, often with clubbed feet, sometimes with hydrocephalus and hypertrichosis.

Other causative factors have been thought to be an abnormally large size of the pelvis, an enlargement of the uterine body or cervix or of the entire organ, and increased abdominal pressure; such a case for example as that of Stepkowski,[4] who saw a woman, aged twenty-five years, with complete prolapse of the uterus and vagina

[3] Cyclopedia of the Diseases of Children, Keating and Edwards.
[4] Gaz. lek in Przegl. Chir., la Gynic., 1897, No. 1.

which was caused by excessive vomiting when she was but thirteen years of age, and that of Karczewski,[5] who saw a girl, aged thirteen years, with complete procedentia developing gradually from carrying heavy burdens. Uterine displacement other than prolapse also occurs in very young children. Spencer[6] reports a case of retroflexion of the uterus in a newborn child, and Berli,[7] one of congenital displacement in the newborn. Carpenter,[8] who was one of the pioneers in the rectal examination of children, says that a uterus in a child, aged about two years, is an inch long and an inch broad at the fundus, the tubes about one and three-fourths inches, the right ovary five-eighths inch in length, and the left one-half inch in length, and each about one-sixth inch in diameter. The ovaries vary from five-sixteenths inch long by one-fourth inch broad in a child a few weeks old. The organs measure one and one-half inches by one-half inch in a child approaching puberty. Ovaries show some variations in size in children of similar ages. One ovary is not infrequently decidedly larger than its fellow. The Fallopian tubes for clinical purposes are about equal to the vas at a similar age, at their narrowest part, but they gradually enlarge as they pass along to the fimbriated extremity; in length they vary from a little over one inch to a little over three inches, according to age.

As I have already stated, the two anatomical aids to the recognition of these structures when examining by the rectum are the iliac arteries and the uterosacral ligaments. These ligaments, as Keating and I showed many years ago, form a curve surrounding the rectum in children, and when the finger is introduced and passed gently upward their sharp edge is readily recognized. Following up this edge we surely come to both the tube and the ovary which can be outlined by pressing toward the bony wall of the pelvis. The ureters are also palpable under the same guidance; in this way an impacted calculus has been detected in a tuberculous ureter in a child.

In examining children we must ever bear in mind that displacements of the ovaries and tubes into the inguinal or crural openings are not extremely unusual, and if we find difficulty in locating them in the pelvis, these latter structures, the navel, the ischiadic, and obturator foramina should be examined; it is well also to remember that these prolapsed ovaries may be cystic and cause considerable difficulty in diagnosis.

Diseases of the uterus, tubes, ovaries, and vagina in childhood are far more frequent than is generally supposed by those who have not given special attention to the study of those diseases in the very young. Even as late as 1888 no less an authority than Lusk[9]

[5] Gaz. lek in Przegl. Chir., la Gynic., 1897, No. 1.
[6] Trans. Obstet. Soc., London, 1892–93, xxxiv, 25 to 28.
[7] Univ. Med. Mag., 1893–94, vi, 185.
[8] Pediatrics, 1896, i, 481
[9] American System of Gynecology.

wrote that no case of uterine sarcoma is known to have occurred previous to puberty, a statement as incorrect then as it is now. The literature on this subject, for the most part, is scattered throughout periodical publications, but of recent years Howard A. Kelly and I have made an attempt to consolidate these scattered publications into standard text-books.[10]

To show the frequency of pelvic disease in children it is only necessary to say that Bland Sutton has recently collected one hundred cases of ovariotomies performed on children under sixteen years of age. Weil[11] has added sixty cases under ten years of age, and I have over 275 references to pelvic and abdominal diseases in little children. But to those of us who have engaged in this study for a number of years, the manner in which writers report their cases is extremely disappointing, when we are endeavoring to elucidate new facts. Because pediatrics as a special department is new, it is most important to record every detail in the clinical history and in the operative procedures, but most important of all is the later history of the patient, as by this knowledge alone shall we be able to formulate the factors upon which to base reliable conclusions both as to the immediate prognosis and the expectancy.

An interesting point is that all forms of diseases of the adult female pelvis have been recorded in childhood. Again, in the child certain growths seem to have certain selective age periods: sarcoma and dermoids usually occur under the third year; and ovarian cysts become more frequent about puberty, although they are seen at all ages, even from the earliest infancy. Chiene[12] removed one at the early age of three months; Boullard[13] saw a newborn infant in whom both ovaries contained a large number of cysts; Schultz[14] saw an ovarian cyst in a still-born child; Doran[15] reported proliferating cysts in the ovary in a seven-months fœtus; and Lederer[16] operated upon a fifteen-weeks-old infant for cystic degeneration of the left ovary and in addition found the right ovary in the inguinal canal. Some very early successful cases of removal of sarcoma of the ovary are recorded: Harris,[17] for example, removed such a tumor in a child, aged twenty-two months; Hoffman's[18] patient was aged thirty-three months (fatal result); Cameron's[19] was forty months old (also fatal result). Byford[20] had a successful case at the age of four years and eight months. Altogether a large number of sarcomatous ovaries have been observed and recorded in children from an early age

[10] Cyclopedia of Diseases of Children, Keating and Edwards, first, second, and third editions, 1889 to 1901, J. B. Lippincott Co., Philadelphia, Pa.; Gynecology and Abdominal Surgery, Kelly and Noble, vol. i, p. 809, W. B. Saunders & Co., 1907, Philadelphia, Pa.

[11] Johns Hopkins Hospital Bulletin, March, 1905, xvi, No. 168.

[12] Edin. Med. Jour., June, 1884.

[13] Bull. soc. anat. de Paris, 1854, xxix, 15.

[14] Verhandl. d. Gesellsch. f. Geburtsch. in Berlin (1857–58), 1859, xi, 55 to 57.

[15] Proc. Path. Soc. London, 1880–81, xxxii, 147 to 150.

[16] Allg. Wein. Med. Zgt., 1895, x, 253.

[17] Amer. Jour. Obst., October, 1904, 530.

[18] Ibid., xxxvi.

[19] Glasgow Med. Jour., 1889.

[20] Chicago Med. Record, 1891–92, ii.

up to about the eighteenth year (see Tables I and II)—a later age excluding their study for this paper. Nor is carcinoma of these structures unknown during the earlier years of life: Brown[21] reports one encephaloid disease of the right ovary in a child (age not stated); Marjolin's[22] remarkable case was aged but one year, but had a very large cancerous tumor. Weil[23] reports an adenocarcinoma of the left ovary in a girl, aged five years. The ovary was the size of a large cocoanut, freely movable, and was removed with the left tube without any hemorrhage. The child made a remarkable recovery. Stolypinsky[24] reports a carcinoma of the ovary in a girl, aged eight years; Leopold[25] one in a girl aged nine years; Corse[26] one involving the uterus and ovaries in a girl, aged twelve years, and Michel[27] removed by operation a carcinoma of the ovary that was the size of a man's head, in a girl aged sixteen years. In two years she died of recurrence. At autopsy a large tumor in the left side of the abdomen was found, with metastasis to the liver and kidneys, but most interesting of all is the fact that the microscope showed the tumor to have a chorion-epithelioma-like structure.

Many more instances of the early involvement of the ovary by malignant disease could be cited from the literature, but sufficient has been given to make good my contention that the disease can no longer be considered extremely rare, even at the very early periods of life.

Let me briefly consider the clinical modification in the disease due to the tender age of the subject. The age, by the way, is absolutely no contra-indication to operation. It is true that the very young do not stand this sort of surgery as well as the very old; nevertheless their resistance is surprisingly good and sufficiently reliable to warrant extensive surgery in the face of malignant involvement of removable structures. Malignant ovarian tumors are more common in children than in very old women; of these, the ovarian dermoids and sarcomas are perhaps the most frequent. We must not forget the presence of carcinoma at this period of life. Many of the earlier cases are no doubt rather carelessly worked out in regard to the microscopic diagnosis. Cullen says that adenocarcinoma of the ovary is extremely deceptive unless many sections from the various parts of the growth are examined and then it will be found that the advancing edges are most characteristic of the carcinomatous arrangement.

[21] Lancet, London, 1858, i, 456.
[22] Bull. soc. de chir. de Paris (1860), 1861, 2 s. 1, 667–72.
[23] Ibid.
[24] Rev. de gynecol. et de chir. abd., viii, 708.
[25] Centralbl. f. Gyn., 1874, xviii.
[26] Trans. Coll. Phys., Philadelphia (1856–62), 1863, n. s., iii, 336
[27] Zentralbl. f. Gynäk., 1905, No. 14.

The symptoms of a malignant pelvic growth in a child are very likely, in my experience, to be extremely indefinite. Certainly this is so in the earlier stages and in the two cases of which I have notes, the sarcoma of the ovary had reached such a size as to be noticeable externally and the parents discussed the change of contour in the abdominal segment; but the children denied all abnormal abdominal sensations. Neither of these children had emaciated at all, and were brought to me because they had a large growing abdomen.

If we are unable to satisfy ourselves that the diagnosis is complete and that malignant disease or other serious pelvic abnormalities do not exist, there can be no possible objection to an exploratory incision in the child when life seems threatened by an abdominal growth. If possible, one should remove the growth at this time; if not, the simple incision carefully made and carefully attended to afterward does not add to the danger of the already existing disease. I always prefer the median incision in children, made one inch above the symphysis pubis and extending upward one and one-half to two inches.

This incision renders all the organs accessible, and its closure is perhaps less subject to hernial complications. The peritoneum in the child is a very delicate membrane; it should be picked up in a fold and very slightly nicked, when air will enter the general cavity and the incision may be cautiously enlarged. It may be torn the full length of the incision, but I prefer the use of scissors. The entire pelvis, contiguous and related organs, should be carefully and systematically explored. My rule has been the uterus first, because it is more readily recognized, then the right and the left palpation of ovaries, tubes, broad ligaments, ureters, kidneys, and appendix. This can be very gently and quickly done in the child, and with but little manipulation, so accessible are the organs. Of course, very simple means should be employed first, but I never hesitate to advise exploratory incision if the diagnosis is not perfectly clear or if there is any question at all of malignancy.

In the child, unlike the adult, the abnormal pelvic conditions are always of a serious nature. An abdominal tumor in a child is likely to be either a dermoid cyst, sarcoma, or adenocarcinoma of the ovaries, malignant or cystic renal diseases, or certain somewhat rare and atypical retroperitoneal renal disorders. So we must of necessity look upon the presence of an abdominal tumor in a child as of serious import, and exhaust all methods of arriving at an accurate diagnosis.

Henning's[28] treatise, written nearly thirty years ago, is still the best on the diseases of the female sexual organs in children. He tells us that dermoid cysts are apt to be carried into the years of puberty, on account of their slow growth and lack of early symptoms;

[28] Gerhardt's Handbuch der Kinderkrankheiten.

TABLE I.—Malignant Disease of the Ovary in Children.

Reporter	Age	Tumor	Remarks	Reference
Doran	7 mos. fœtus	Cancer	.....	Trans. Path. Soc., London, 1882
von Franqué	fœtus	Sarcoma	.....	Weil; Johns Hopkins Hosp. Bull., March, 1905, No. 168
Hollander	9 mos.	Spindle- and round-cell sarcoma	Operation: recovery. This case appears also in Table II	Deut. med. Woch. Vereins, Beilage, 1896, xxii, 16; Ped. 1896, ii
Marjolin	1 yr.	Cancer of ovary	Very large	Bull. soc. de chir. de Paris (1860) 1861, 2 S., i, 667-672
Harris	1 yr. and 10 mos.	Sarcoma and endothelioma	Recovery; twisted pedicle	Amer. Jour. Obstet., October, 1904
Pick	2 yrs.	Spindle-cell sarcoma	Vagina and all pelvic organs infiltrated	Arch. f. Gynäk., 1894, xlvi, p. 592
Gibb	2½ yrs.	Cystic sarcoma	.....	Glasgow Med. Jour., lx, No. 1, p. 33
Evers	2½ yrs.	Sarcoma	.....	St. Louis Courier of Med., August, 1884
Hoffman	2 yrs. 9 mos.	Sarcoma	Death	Amer. Jour. Obstet., xxxvi
Cameron	3 yrs. 6 mos.	Sarcoma	Death	Glasgow Med. Jour., 1889
Smith, F. C.	3 yrs.	Myxosarcoma	Recovery; vaginal and uterine polyps, uterine subperitoneal growth. This case also appears in Table II	Ibid
Schwartz	4 yrs.	Adenocystoma	Recovery	Arch. f. Gyn., xiii, 4
Foerster	4 yrs. 6 mos.	Sarcoma	Death	Amer. Jour. Obstet., xxxi
Byford	4 yrs. 8 mos.	Sarcoma	Recovery	Chicago Med. Rec., 1891-2, ii
Weil	5 yrs.	Adenocarcinoma	Operation; recovery. Tumor size of a cocoanut; removed with tube; no hemorrhage; alive and well at time of report	Johns Hopkins Hospital Bull., March, 1905, xvi, No. 168
Demme	5 yrs.	Congenital fibrosarcoma	.....	Jahrsb. des Jennerschen Kinder spetales ze Berne, 1881
Turner	6 yrs.	Medullary sarcoma of both ovaries and of peritoneum	Death	Trans. Path. Soc., London, 1892-3, xliv, 110
Page	6 yrs.	Sarcoma	Recovery	Lancet, December, 1895
Parry	7 yrs.	Carcinoma	Death	Lancet, 1907, ii, 1607
Croom	7 yrs.	Sarcoma	Recovery; last report two years later; still well. Croom considers premature sexual development in relation to ovarian tumors	Edin. Med. and Surg. Jour., 1893, p. 689
Olshausen	8 yrs.	Carcinoma	Autopsy; no operation	Weil, Ibid
Stolypinsky	8 yrs.	Carcinoma	Result not stated	Rev. de gyne. de chir. abdom., viii, 708
Gussenbauer	8 yrs.	Carcinoma	Recovery	Wien. med. Woch., 1894, No. 41
Sharp, W. H.	8 yrs.	Cystic encephaloid	Not stated	N. Y. Med. Jour., 1874, xix, 52-54
Chenoweth	8 yrs.	Sarcoma	Recovery	Amer. Jour. Obstet., xv
Malius	9 yrs.	Cystosarcoma	Death	Lancet, 1890, i, 1174
Forbes	9 yrs.	Myxosarcoma	Recovery	Australian Med. Jour. Melbourne, 1894, xvi
Leopold	9 yrs.	Carcinoma	Death	Centralblatt f. Gynäkologie, 1894, xviii
Palmer	9 yrs.	Cancer	.....	Trans. Med. Soc., Dist. Columbia
McBurney	10 yrs.	Sarcoma	Recovery	Annals Surg., 1895, xxi, 706
Wagner	10 yrs.	Sarcoma	Recovery	Arch. f. klin. Chir., xxx, 704
Croom	11 yrs.	Sarcoma	Recovery	Obstet. Trans. Edin., xiv, 93

Reporter	Age	Tumor	Remarks	Reference
Edwards, Wm. A.	11 yrs.	Sarcoma	Recovery; child made excellent operative recovery; died in six weeks from general metastasis	Present communication
Kelly, H. A.	12 yrs.	Sarcoma	Perfect recovery; tumor large enough to fill a hat; died 2 years later from dysentery	Cyclop. Dis. of Children, Keating and Edwards, iii, 739
Eckhardt	13 yrs.	Sarcoma	Recovery; double oöphorectomy as opposite ovary was cystic; 1½ years later showed no recurrence	Deut. med. Woch., 1895, S. 96
Bode	13 yrs.	Sarcoma	Recovery; tumor filled entire abdomen; grew under sheath of abdominal muscles	Central. f. Gyn., Bd. xviii, 1171
Anderson	13 yrs.	Sarcoma	Recovery; died in few months from recurrence	Bland Suttou., Diseases of Tubes and Ovaries
Marien	13 yrs.	Sarco-epithéliome	.....	Univ. Méd. du Canada, Montreal, 1908, xxxvii, 317-320
Joüon	13 yrs.	Tumeur maligne de l'ovaire	Recovery	Gaz. med. de Nantes, 1907, 2, S., xxv, 17
Smith	13 yrs.	Carcinoma	Death; both ovaries diseased	Lancet, 1874, ii, 501
Gage	15½ yrs.	Sarcoma	Recovery; tumor filled abdomen and very adherent	Jour. Amer. Med. Assoc., December, 1894
Thornton	15 yrs.	Carcinoma	Death	Med. Times and Gaz., 1883, i, 211.
Von Szabo	15 yrs.	Carcinoma	Death; hemorrhage into abdominal walls and intestinal adhesions	Arch. f. Gyn. Bd. xxxii, S. 193
Michel	16 yrs.	Carcinoma	Recovery; died in 2 years from recurrence; growth size of man's head removed at operation; autopsy, large tumor on left side of abdomen; metastasis to liver and kidneys; microscope showed that the tumor had a chorionepithelioma-like structure	Zentralbl. f. Gynäk., 1905, No. 14; Amer. Med., August 26, 1905, p. 377
Homans	17 yrs.	Sarcoma of pelvic organs, omentum and mesentery	Died of shock in three hours; about 13 pounds of encephaloid cancer removed	384 Laparotomies for Ovarian Disease; Sawyer & Sons, Boston, 1887
Binaud	17 yrs.	Primary (large) cancer of ovary	Perfect recovery; cancer was very voluminous(3 lb. 7,oz.) with ascites; a perfect cure by ovariotomy	Jour. med. de Bordeaux, 1894, xiv., 345
Donhauser	Children	Malignant ovarian tumor	.....	Albany med. Ann., 1906, xxvii, 20–30
Mo. G.	Child, age not stated	Sarcoma	Death	Osservatore, Torino, 1876, xii, 84
Fenemenow	Child, age not stated	Sarcoma	Death	Rev. de gyn. et de chir. abdominale, 1904, viii, 708
Piwowarski	Child,	Malignant ovarian tumor	The author considers this to be a rare tumor	Ueber einen seltinen Fall von malignen Ovarialtumor bie einen Kinde, Berlin, 1905, xliv, 8
Brown	Child, age not stated	Encephaloid of ovary	.....	Lancet, 1858, i, 456
Amann	Child, age not stated	Carcinoma	Exploratory incision	Weil, Ibid

TABLE II.—Malignant Disease of the Uterus in Children.

Reporter	Age	Tumor	Remarks	Reference
Hollander	9 mos.	Sarcoma of uterus and vagina	Total extirpation; discharged from hospital in 1 month, cured	Deut. med. Woch., 1896, xxii, 16
Curtis	12 mos.	Sarcoma of cervix and vaginal vault	Operation; death following day	Trans. Obstet. Soc., London, 1904, xlv, 320
Findley	18 mos. first noticed	Primary, small spindle-cell sarcoma of cervix	First noticed on anterior lip of cervix; removed; in 6 weeks return; in 3 months another operation; child died in fourth year of life; whole pelvis filled with mass	Surg., Gynec. and Obstet., Chicago, 1906, iii, No. 4, p. 501
Rosenstein	2 yrs.	Carcinosarcoma	Died	Arch. f. path. Anat., Berlin, 1883, xcii, 191
Steffen	From 5 mos. to 2 yrs.	Eight cases; 3 sarcoma of uterus; 2 carcinoma of uterus; 3 sarcoma of uterus and vagina	All the sarcomas were considered to be congenital; Steffen says that benign congenital tumors are known to become malignant after attempt at radical removal	Die Malignen Geschwülste in Kindesalter, 1905
Virchow's Arch.	Less than 2 yrs.	Primary sarcoma of fundus uteri; extensive in bladder	Death from cachexia	Virchow's Arch., Bd. xcii, 1
Pick, L	2 yrs.	Primary carcinoma of cervix	Polyp in vagina; secondary large growth in abdomen; death due to chronic peritonitis	Arch. f. Gyn., Bd. xlvii, 1
Laidley	2 yrs. and 6 mos.	Carcinoma; post-mortem and microscopic diagnosis	Death	St. Louis Courier of Med., Sajou's Annual, 1891, F. 34, vol. ii
Smith, F. C.	3 yrs.	Small round-cell myxosarcoma of uterus	Subperitoneal uterine growths; vaginal polyp; death in 33 days after removal of vaginal growth	Amer. Jour. Obstet., 1883, xvi, 555–6
Ahlfeld	3 yrs. and 6 mos.	Sarcoma probably primary in vagina; a large tumor was attached to the fundus uteri and occupied the entire cavity of the uterus	Posterior wall of bladder involved	Arch. f. Gyn., Band xiv, 1
Depage	3 yrs. and 6 mos.	Primary sarcoma of uterus; microscopic diagnosis	First operation for cervical fibroid; growth recurred in 6 months; vaginal hysterectomy; in 6 weeks entire pelvis involved; death	Central. f. Kinderheilk., 1902, Bd. vii, S. 103
Markovic	5 yrs.	Large sarcoma of posterior wall of uterus	Death	Liecnieki, 1901, xxiii, ii, 426
Gynghofner	8 yrs.	Anterior lip of cervix growth size of a hazel nut; medullary carcinoma	Almost continuous hemorrhages from genital tract for 2 or 3 years; died	Ztsch. f. Heilk. Prag., 1888, Band ix, 4–5 S. 337, 1 pt
Homans, J.	10 yrs.	Cancer of abdominal organs	Recovered from operation; died 9 months later	Laparotomies for Various Diseases, Sawyer & Sons, Boston, 1887
Bluhm	11 yrs.	Sarcoma; cervical polyp		Arch. f. Gyn., Band lxviii, Heft 62
Agnus Bluhin	11 yrs.	Sarcoma botryoides mucosacervicis	Operation; recovery	Med. Woch., iv, 21, No. 175, Mai 25
Zweifel	13 yrs.	Round-cell sarcoma of uterus	Death	Cent. f. Gyn., 1884, Band viii, S. 401
Von Konig	13 yrs.	Krebsbildung	Died	Allg. Wien. Med. Ztg., 1885, xxx, 280
Wells	13 yrs.	Cancer of body of uterus; extension to bladder	Menses suppressed for 8 months, then uterine hemorrhage which persisted until death	Findley, Surg., Gyn., and Obstet., Chicago, 1906, iii, 502

Reporter	Age	Tumor	Remarks	Reference
Little	14 yrs.	Carcinoma of cervix uteri		New Orleans Med. and Surg. Jour., 1896–7, xlix, 322
Jaeger	15 yrs.	Fibrosarcoma of uterus		Central States Med. Monit., Indianap., 1906, ix, 754
Bracts	18 yrs.	Tumor of posterior lip of cervix, 2 cm. in diameter	Kaltenbach removed the uterus by vagina; girl died in 4 weeks; no autopsy; growth was thought to be an endothelioma	Arch. f. Gynäk, Bd. ii, 1896
Coppée	18 yrs.	Encephaloid cancer of rapid growth	Death	Bull. soc. de méd. Gand., 1864, xxxi, 35–39
Tschop	19 yrs.	Carcinoma; microscopic studies	Vaginal hysterectomy; full recovery; vagina and adnexa not infiltrated	Central. f. Gynäk., 1897, No. 2
Pick, L.	Children	Sarcoma of uterus and vagina		Ueber Sarcome des Uterus und der Vagina in Kindersalter und des Primäre Scheidensarcoma des Erwachsenen; Arch. f. Gynk., Berlin, 1894, xlvi., 191–255
Odebrecht	Young, age not stated	Sarcomatous degeneration of a uterine myoma	Recovered	Zent. f. Gynäk., 1904, No. 2
Chase	Young, age not stated	Sarcoma of uterus and ovaries	Mixed toxin treatment	Brooklyn Med. Jour., 1896, x, 442
Marsh	Child	Sarcoma of uterus	Vagina and rectum involved	Findley; Surg., Gyn. and Obstet., Chicago, 1906, iii, 502

indeed, the growth may be so slow that their presence may not be manifested until adult life is reached. In the meantime the ovary will functionate normally. Ovarian cysts, on the other hand, are brought to us while the child is still quite young; it may be as young as three months. Malignant disease of the organs develops very rapidly in the child, and is likely to be accompanied by ascitic fluid; but my experience is that the general health does not become involved as early as we would suppose. Most writers say that it is characterized by early marked affection of the general health. This is certainly not so in my cases. The children with malignant abdominal growth were brought to me because their parents recognized the abdominal enlargement, and not because the child's symptoms were exacting, although in two instances the growths were very large. Of course, later the symptoms are those common to all malignant growths, whether in child or adult.

Sarcoma is the most frequent growth found in the child's ovary. Most of the congenital growths are sarcomas, and they have a strong histological resemblance to embryonic ovarian stroma. Most of those in infancy and childhood are made up of small round cells. The other varieties described in children are: Spindle-cell sarcoma, lymphangioma, endothelioma, and fibrosarcoma.

Emanuel's[29] case of tumor of the left ovary, in a fifteen-year-old

[29] Zeit. f. Geb. u. Gyn., Band xxv.

girl, contained tissue elements of endo-, ecto-, and mesoderm, but its stroma was sarcomatous. The child made an excellent operative recovery, but died four months later from recurrence.

The prognosis of malignant growths of the ovary at the present time is rather appalling. This is due, however, to the fact that the cases are not submitted early enough to radical removal of the incipient growth. The age of the child has little to do with it; very young children have recovered from abdominal operations of all sorts. I agree with Baginsky that the prognosis becomes better day by day as the technique of operations in this region progresses; as a writer has said, the age of the patient does not, as one would suppose, contribute any valid reason for refusing to operate; and, as Kelly says, on account of the large percentage of malignant tumors in children and the consequent dangers of delay, the operation should be performed as soon as the patient can be suitably prepared for it. Henning recognized twenty-seven years ago the advantage of early operation in children.

If the tumor is a dermoid or cyst the prognosis is extremely good, even at the most early age of infancy; but if it is sarcoma or carcinoma the operative prognosis at the present time is appalling and the chances of non-recurrence are remote. Thus, of Sutton's 21 cases of ovarian sarcoma, 11 died within a year after their operations, a mortality of 52.4 per cent. The mortality in cysts will be about 8 per cent., in dermoids, between 13 and 21 per cent.; and in solid tumors (malignant), between 33 and 52 per cent. The literature, however, contains a number of examples in which the children survived for years and were well when last heard from. Bode's[30] case of a girl, aged thirteen years, with large round-celled sarcoma of the right ovary, growing under the sheath of the abdominal muscles, was in perfect health four years after its removal. Gage[31] removed a two and one-half pound, round-cell sarcoma from a fifteen-year-old girl, who five years afterward was well and married. Kelly's patient with ovarian sarcoma, aged twelve years, lived two years after operation and died from dysentery, without return of growth. Harris's case of twenty-two months of age recurred, as did Byford's, aged four years and eight months, Page's,[32] a six-year-old girl, Croom's,[33] a seven-year-old girl, Forbes'[34] at nine years, McBurney's[35] at ten years, and Wagner's[36] at ten years. The record in carcinoma in children is most unsatisfactory, with here and there a gleam of hope. Redner's case, a nine-year-old child, died one year later from recurrence. She made a good operative recovery. One of this operator's cases in a child was well four years after the removal of the ovary; another of the children died in three months from

[30] Central. f. Gyn., Band xviii, S. 1171.
[31] Jour. Amer. Med. Assoc., December, 1894.
[32] Lancet, December, 1895.
[33] Edin. Med. and Surg. Jour., 1893, p. 689.
[34] Australian Med. Jour., 1894, xvi.
[35] Annals of Surgery, 1895, xxi, 706.
[36] Arch. f. klin. Chir., xxx, 704.

recurrence. Homan's[37] case, aged ten years, of cancer of the abdominal organ recovered nicely from the operation, but died nine months afterward from recurrence. Michel lost a case in a sixteen-year-old girl two years after operation from recurrence in the liver and kidneys. Weil's case of adenocarcinoma of the ovary at five years of age was well at the last report, March, 1905.

In true carcinoma of the uterus in children our therapeutic measures are as yet of little avail. Rosenstein's[38] case, aged two years, classed as a carcinosarcoma of the uterus, died fourteen days after operation. Ganghofner's girl, aged eight years, with a uterus 2.6 cm. long, containing a cancerous tumor the size of a crown piece, died from an intercurrent variola. Blum's[39] case, aged eleven years, with sarcoma of the cervix, died from recurrence. Agnus Bluhin's[40] case of sarcoma botryoides cervicis in an eleven-year-old girl recovered. Bradford's[41] case, a girl aged nine years with papillary cystoma, the size of the head of a full-term fœtus, was well three months after a complete hysterectomy. Odebrecht's[42] case in a young girl (age not stated), with sarcomatous degeneration of a uterine myoma recovered after operation. Worrall's[43] case of adenoma of the uterus and double ovarian tumor recovered completely. I do not know the termination of Little's[44] case of carcinoma of the cervix uteri in a fourteen-year-old girl, but imagine it too was fatal.

Of the greatest interest are the cases of chorio-epithelioma in children, the so-called deciduoma metastica malignum of Sänger. Schlangenhofer, of Vienna, in 1902, reported one in a virgin, aged thirteen years, who had never menstruated; Ahlfeld[45] one at seventeen years of age; and Champneys[46] one at eighteen years; while Brock's[47] case was a mole passed by a girl twelve and one-half years old. It has been aptly said that a mother fatally invaded by the trophoblast of her own child would be a person of one generation killed by a tumor belonging to a person of the next generation—a matricide; but these little girls slain by an embryoma in their own uterus are the victims of a potential brother or sister, not of their own child. It is now a fratricide.

For purposes of illustration I will detail the notes of but one case of malignant disease of the ovary.

A. B., aged eleven years, was brought to me on May 20 by her father, because he noticed a reluctance on the child's part to go through the "setting up" exercises which it was the custom of the

[37] Three Hundred and Eighty-four Laparotomies for Various Diseases, 1887.
[38] Arch. f. path. Anat., 1883, xcii, 191.
[39] Arch. f. Gyn., Band lxviii, Heft 62.
[40] See table.
[41] Arch. Pediat., 1892, ix, 508.
[42] Zent. f. Gynäk., 1904, No. 2.
[43] Australasian Med. Gaz., Sydney, 1893, xii, 308.
[44] New Orleans Med. and Surg. Jour., 1896–97, p. 322.
[45] Monatsschr. f. Geb. u. Gyn., 1895, i.
[46] London Pract., January, 1896.
[47] Stone, Chorio-epithelioma, Amer. Jour. Obst., October, 1907.

other children to do every morning. This child said it gave her an uncomfortable sensation to stoop forward and touch the floor with her hands. This was the only symptom that she complained of. There is absolutely nothing of interest in the previous history of the child or in the family history. The mother thought the child's waist measure was increasing. Examination at this time showed a large tumor occupying the right iliac, lumbar, and hypogastric region to the line of the umbilicus. The tumor mass was rather movable. It was readily outlined and was apparently extrapelvic; that is, it did not seem to have a pelvic origin; its physical signs were rather those of kidney enlargement, but the urine was absolutely normal and remained so. The inguinal, axillary, and cervical glands were not enlarged. The mammæ were normal and the pubic hair was not developed. The edge of the tumor was easily outlined.

In a few days (May 24) the temperature became slightly elevated and irregular, ranging between 99.3° and 100° F. This continued up to the time of operation, the temperature occasionally but rarely below the normal. This fall might occur in the morning or the evening; its time of elevation was irregular also. The highest temperature recorded from the first observation, May 20, to the date of operation, June 18, was 101.2°, which occurred on May 27, and seemed to be due to an intestinal toxemia. The lowest temperature was 98.2° F. During the pre-operative period of observation, extending over twenty-nine days, the child not only did not lose weight, but gained one pound between May 24 and June 7.

Operation: Right salpingo-oöphorectomy, with the coöperation of Drs. Lasher, Dunbar, Magee, and Parsons; ether was used and 65 grams was administered. The operation consumed thirty-eight minutes and the anesthesia forty-five minutes. Median incision. The growth was found to be a large sarcoma of the right ovary. A portion of it was wedged tightly between the uterus and the bladder, the adhesions being very intimate, but easily broken up. There was some free hemorrhage. The major portion of the growth was above the brim of the pelvis and occupied about the site of an enlarged kidney; its contour was not unlike that organ. The portion that extended out of the pelvis was pedunculated. The uterus was not enlarged. There was no evidence of metastasis at the time of operation. The child was shocked somewhat during the removal of the growth, but readily responded to the usual methods of combating such a condition.

The child had an absolutely uneventful convalescence, suffered little pain, and speedily arose from bed. Within a month a return of the growth was noted in the abdomen, and in six weeks the child succumbed to what seemed to be the most extensive involvement of the organs in the abdomen that I have ever seen. At the post-mortem, metastasis was seen to be universal; no structure seemed to have escaped its invasion.

Primary tumors in the vagina are rare at all ages; they are usually

fibroma, fibromyoma, myoma, sarcoma, or carcinoma. All except the last two are very rare in children, and these even are of very infrequent occurrence. Sarcoma of the vagina, however, is more frequent in children than in adults; in one of the series in the literature, that of Starfinger, of 26 cases, 24 were in children under five years of age; indeed, 10 were under one year of age. Malignant disease of the vulva and vagina constitutes but 1 per cent. of all malignant disease of the genital tract at all ages. The growths may apparently be congenital or appear early in life, before the fifth year, many, in fact, before the first year. They may develop from the walls of Gärtner's canals or from an obliterated Müller's duct. Primary sarcoma of the vagina is the most frequent malignant growth in childhood and is a specialized form of malignant disease which may affect any or all of the connective tissues which are involved in the complicated developmental processes associated with the formation of cloaca. Sarcoma of the vagina in childhood is usually microscopically the characteristic structure of racemose sarcomas. Striated muscle fibers are sometimes seen in the primary tumor, the secondary growths, and in the metastases, fibers which Piquand[48] says resemble the striated muscle found in a three-months' fœtus. The sarcoma usually grows in the connective tissue of the pelvic organs, and may extend in all directions, into the uterus, vagina, bladder, and urethra. In some cases it may remain circumscribed in the vagina; its usual clinical form, however, is that of a polyp, either vaginal or uterine, often both.

In children vaginal sarcoma shows very distinctly this tendency to become pedunculated, polypoid, and multiple. It pursues a comparatively slow growth and ulcerates very slowly, if at all; the lymphatic glands are affected, if at all, late in the case, and in consequence it dissiminates very slowly. The growth may be so slow that Herndon,[49] who has written a most valuable article on the pathology of the reproductive organs, thinks that the tumors that were not observed until the sixth and fifteenth years, respectively, are probably congenital, but do not show active growth until this later period.

There is usually little trouble in making the diagnosis, but unfortunately the general practitioner is apt to look upon the polyps as benign growths, and the diagnosis is then not made until it is too late to remove the entire growth. The prognosis at best is grave, but recently some happy results have been reported, cures lasting for several years (see Table III), as much as ten in one instance, without recurrence, the children then passing from observation. Unfortunately, however, recurrence and speedy recurrence is still the rule, and the children die early from malignant toxemia or from pressure on the bladder and rectum and absorption toxemia.

[48] Sarcoma of the Uterus, Rev. de gyn., 1905, ix, 579.
[49] Kelly and Noble, Gynecological and Abdominal Surgery, i, 98.

TABLE III.—Malignant Disease of the Vagina in Children.

Reporter	Age	Tumor	Remarks	Reference
Heckford	2 mos.	Vaginal and vulval villous tumor, "medullary"	.....	Trans. Obstet. Soc., 1868, x, 224
Hauser	6 mos.	Vaginal tumors; multiple; anterior vaginal wall	Round and spindle-cells and striped muscle fibres; operation; recurrence at short intervals; death	Virchow's Archiv., Bd. lxxxviii, S. 168
Rabe	6 mos.	Tumor size of small nut at site of vestibule; involved urinary meatus; sarcoma	Removal of uterus and vagina by laporotomy; death from bronchopneumonia	Surgeon General's Catalogue, Holmes, Pediatrics, 1907, xix, No. 2, 99
Frick	7 mos.	Right anterior vaginal wall; round and spindle-cell sarcoma	Operation; rapid recurrence and death	Surgeon General's Library, Holmes, Ibid
Schuchardt	7 mos.	Vaginal tumor	Mixed-cell sarcoma; operated on by Volkman; at report cure had lasted 10 years	Verhandl. der Deut. Gesellsch. f. Gynäk. 1868, Bd., ii, S. 239
Hollander	9 mos.	Vaginal polyp; large	Posterior wall of uterus also involved; spindle and round-cell sarcoma; operative cure by Israel	Deut. med, Woch., Vereins Beilage, 1876, xxii
Johannersen, A.	11 mos.	Sarcoma	Whole pelvis involved	Jahrb. f. Kinderh., 1897, N. F. xliv, 114–122
Kolisko	12 mos.	Left vaginal wall, number of large and small polyps; round and spindle-cell sarcoma	Repeated operation, with rapid recurrence after each; death 6 months after first noticed from pyometritis and suppurative peritonitis	Wien. klin. Woch., 1889, ii, 109, 130, 159, 182, 202, 222; Kolisko abstracts twelve other cases from the literature and thinks that early and radical extirpation of primary tumor justifies hope for successful issue
Weinlechner	12 mos.	Vaginal polyps: sarcoma	.....	Wien. klin. Woch., 1889, S. 109
Holmes, O. L.	17 mos.	Round-cell sarcoma; anterior vaginal wall	Three incomplete operations; death due to uremia and septicemia	Trans. Med. Assoc., Georgia, Atlanta, 1906, 304–311; Pediatrics, N. Y., 1907, xix, 95–100
Starfinger	18 mos.	Large round and spindle-cell sarcoma posterior vaginal wall	Removal by curette; death in 3 weeks; duration of disease 6 months	Steinthal, Virchow's Archives, Bd. iii, S. 449
Thomas	18 mos.	Tumor of left labium majus; sarcoma	.....	Amer. Jour. Obstet., vii, 51
Strassman	18 mos.	Patly gangrenous tumor protruding from vagina; large round and spindle cell sarcoma	Hemorrhage and foul discharge from vagina for 4 months; curretted and tanponned with gauze; result not stated but suggests to remove vagina and uterus per sacrum	Library Surgeon-General's Office, Holmes, Ibid.
Billroth	18 mos.	Fibrosarcoma; warty growth in vagina and bladder	Vesicovaginal septum infiltrated	Wien. klin. Woch., 1889, No. 8, S. 159
Pick	24 mos.	Vaginal tumor; spindle-cell sarcoma	Infiltrating pelvic organs	Arch. f. Gynäk., Bd., 1894, xlvi, 192
Frick	24 mos.	Tumor originated on posterior vaginal wall near vaginal entrance; cylindrical; round and spindle cell sarcoma	Operation; recurrence; sacral operation; tumor same character; recovered and well 3 years after second operation	Holmes, Pediatrics, N. Y., 1907, xix, No. 2
Korner	24 mos.	Vaginal polyps; vesicovaginal septum infiltrated	Fibrosarcoma	Archiv. f. Gynäk., Bd., 1894, xlvi, S. 220, quoted by Pick, Ibid.
Marah	24 mos.	Polyps in vagina and bladder; vesicovaginal septum infiltrated	Small round-cell sarcoma	Trans. Path. Soc., 1874, xxv, 178

Reporter	Age	Tumor	Remarks	Reference
Power	2 yrs. and 4 mos.	Tumor of right wall of vagina; round-cell sarcoma; large portion are fibro-sarcoma and myxo-sarcoma	Admitted to hospital for retention of urine caused by swelling of vagina said to have followed measles 14 months previously; 5 months before admittance polyps noticed in vagina; died of uremia	St. Bartholomew's Hospital reports, xxxi, 121–135; Trans. Path. Soc., xlvii
Schuchardt	2 yrs. and 6 mos.	Vaginal polyp; mixed-cell sarcoma; round and spindle-cells	Some pain and hemorrhage; tumor removed; recurred in 7 months; removed; no recurrence when case was reported	Verhandl. der Deut. Gesellsch f. Gynäk., Bd., 1888, ii. S. 239
Lee	2 yrs. and 6 mos.	Vaginal polyps; vaginal and urethral entrance involved; rectovaginal and vesicovaginal walls involved	Sarcoma; elastic tumor felt in abdomen reaching to umbilicus; died 13 months after first seen	Holmes, Ibid.
Kolisko	18 mos.	Myofibrosarcoma; tumor protruded from vulva for one month before admittance to hospital	No symptoms for 2 weeks; vagina very long; removed tumor, but vagina soon filled again; death; autopsy; origin in anterior vaginal wall; grew to size of walnut in 6 weeks	Wien. klin. Woch., 1889, ii; child was admitted to Billroth's Clinic in 1875 and I think it is the same case as the one that immediately proceeds it in this table.
Kolisko	18 mos.	Polyps; vaginal sarcoma	Died 2 weeks after admission to hospital; autopsy; nodular tumor of vestibule infiltrating vagina, urethra base of bladder and cervix; cystitis, pyelitis, pyelonephritis and pyometra	Ibid.
Weinlechner	18 mos.	Vaginal polyps; myofibrosarcoma	Bladder, cervix and urethra involved	Wien. klin. Woch., 1889, S. 109
Wrede	21 mos.	Cauliflower growth in vagina; round and spindle-cell sarcoma	Removed by ligation; recovered in 2 weeks; repeated operation and recurrences; cystitis, continued fever; death	Holmes, Ibid.
Steinthal	24 mos.	Vaginal tumor; round-cell sarcoma; anterior vaginal wall	Myxosarcoma; duration of disease 12 months; tumor removed after 8 months' duration; recovered in 8 weeks; death in 6 months from uremia	Virchow's Archiv., Bd. iii, S. 449
Piechand, and Guyot	24 mos.	Vaginal tumor on posterior wall; sarcoma	Serious hemorrhage; inoperable on account of size; uterus not involved general suppurative peritonitis cause of death	Holmes, Ibid.
Soltman	2 yrs. and 6 mos.	Vaginal and bladder polyps	Round-cell sarcoma in vagina; spindle-cell in bladder	Jahrb. f. Kinderheilk., Bd. xvi., S. 418
Kelly, H. A.	2 yrs. and 6 mos.	Rhabdomyosarcoma	Death due directly to urinary obstruction	Gynecology and Abdominal Surgery Kelly and Noble, 1907, i, 820
Sathman	2 yrs. and 6 mos.	Anterior vaginal wall and polyps protruding from vagina; round-cell sarcoma	Posterior wall of bladder involved; painful urination; intermittent fever; hemorrhage	Hesterman, Holmes, Ibid.
March	2 yrs. and 7 mos.	Tumor on anterior vaginal wall; polyp	Metastasis on posterior wall of bladder; course of disease 6 months; operation; seven recurrences; death	Hesterman, Holmes, Ibid.

Reporter	Age	Tumor	Remarks	Reference
Marshall	2 yrs. and 7 mos.	Vagina	.....	Brit. Med. Jour., 1889, i, 27
Sänger	2 yrs. and 8 mos.	Polypoid masses in vagina; round-cell sarcoma	Bladder, broad ligaments, deep lumbar glands infiltrated; recurrence in 2 months; death; autopsy; ascites, suppurative peritonitis; large sarcoma; anterior vaginal wall; isolated polyps posterior wall perforating abdominal cavity; dilatation of bladder and ureters	Arch. f. Gynäk., Bd. xvi, S. 58
Brown	3 yrs.	Vaginal sarcoma	.....	Obstet. Soc. of Baltimore, Holmes, Ibid.
Smith, T. C.	3 yrs.	Vaginal and uterine polyps	Myxosarcoma; uterine subperitoneal growths	Amer. Jour. Obstet., 1883, xvi, 555-668; Ibid., 1893, xxvii, 577; when this case was first reported in 1883 it was erroneously considered to be the first case on record
Ahlfeld	3 yrs. and 6 mos.	Vaginal polyps	Fibrosarcoma filling pelvis; inguinal glands enlarged	Arch. f. Heilkunde, Bd., 1867, xvi, S. 135
Schustler	4 yrs.	Vaginal polyps; vesicovaginal septum involved	Myxosarcoma	Wien. klin. Woch., 1888, SS. 148, 225
Demme	5 yrs. and 6 mos.	Vaginal polyps	Fibrosarcoma	Pick (quotes in) Arch. f. Gynäk., xlvi, S. 218
Demme-Gränchier	6 yrs.	Sarcoma	At birth a pea-sized nodule; active malignant growth at 6 years	Gränchier Inaug. Dis. München, 1888
Power, D. A.	Child	Primary sarcoma vagina	.....	Brit. Med. Jour., 1895, ii, 973
Power, D. A.	Children	Primary sarcoma of vagina	.....	St. Barth. Hosp. Report, London, 1395, xxxi, 121, 135
Rollin, M.	Infant	Sarcoma of vagina	.....	Rev. de gynec. et de chir. abd., Paris, 1906, x, 3–20
Peyrache, Jean	Little girl	Malignant tumor of vagina and vulva	.....	Des tumeurs malign de la vulve et du vagin ches la petite fille, Paris, 1905, 101, p. 80
Ward, G. G.	Under 20	Primary epithelioma of the vagina	This seems to be the youngest case on record of primary epithelioma	Contrib. Soc. Med, and Surg. Twenty-fifth Anniv. Founding of N. Y. Postgrad. Med. School and Hosp., N. Y., 1908, 159–166, 1 pt.

As in malignant disease of the ovary, so in similar disease of the vagina, as a rule, the first thing noticed is the tumor; the child's general health is not affected until very late in the disease. The tumor appears between the labia; whereupon the child may complain of some pain, and the evidence of obstruction to urination and defecation will soon become more marked. Another anology is that the nutrition of the child will not be impaired until the disease has progressed to an almost fatal stage; of course, those cases in which the growth early becomes necrotic from pressure will early show the symptoms of septic absorption.

They are said to grow usually from the anterior vaginal wall, but an analysis of the reported cases does not entirely bear out this statement. Carcinoma of the vagina in childhood is still extremely rare. I have elsewhere called attention to Winckel's report of Smith's case of cancer of the rectovaginal wall in a child aged fourteen months; that of Guersant, who saw a carcinoma 20 cm. long and 28 cm. in circumference growing from the introitus of the vagina in a child three and one-half years old. Johannovsky, in the pathological collection at Strasburg, discovered a carcinoma the size of a hen's egg situated in the vaginal vault in a preparation from a girl aged nine years. In the light of present-day knowledge the probability is that these cases classed as carcinoma were sarcoma. Curtis[50] says that there is a case on record of cancer of the vagina in a girl, aged nine years, but he fails to give the reference. Mann has reported two cases between fifteen and twenty years.

Primary epithelioma of the vagina is a disease almost entirely confined to adult life; it is very rare at all ages, and almost unique in childhood. To show the rarity of primary vaginal involvement by cancer it is customary to quote the statistics of W. Roger Williams, who found that of 9226 tumors in the genitalia of women, but 54 were in the vagina. Other statistics bear this out: Reiche, of Hamburg, in 7498 deaths from cancer, found 29 vaginal; Hecht, in 4507 cases, found 50 vaginal. In view of these figures the case of primary epithelioma of the vagina in a patient under twenty years of age, reported by George Gray Ward,[51] becomes of great interest, and will undoubtedly be the cause of further cases being recognized at even earlier periods of life. The girl had never sustained an injury, nor had she been sick at all previous to the discovery of the vaginal growth, which microscopic examination showed to be an infiltrating epithelioma. The growth occurred in the posterior vaginal wall and was inoperable when first seen. It was treated with radium, without result.

The treatment of these forms of malignant vaginal growth is, of course, radically surgical. It must be fully understood that

[50] International Encyclopedia of Surgery, Ashhurst, vii, 293.
[51] Post-Graduate, New York, 1908, vol. xxv.

simple excision of the vaginal polyp, the usual early form of vaginal sarcoma in children, or of the more diffuse tumor growth, will inevitably be followed by recurrence sooner or later, usually soon. After thorough and complete removal a number of children have remained free from the growth for many years; indeed, until they have passed from observation. This is true in Schuchardt's report of a cure lasting ten years; and of Hollander's, after extirpation of the entire genital tract of a child aged two years. Power's patient was free from return for three years, and others for a shorter time. All the cases of carcinoma were fatal.

A CASE OF VIPERINE SNAKE BITE (OF UNDETERMINED KIND) TREATED WITH CALMETTE'S SÉRUM ANTIVÉNIMEUX (OR ANTIVENIN).

By W. F. Arnold, M.D.,
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On October 16, 1908, Mrs. McG., aged twenty years, a native of Georgia, but for twelve years past a resident of Florida, was bitten on the flexor aspect of her right forearm at the junction of its upper and middle thirds, while plucking jessamine blossoms from a tree-like shrub, her arms being extended and raised so that her hands were as high as her face. She felt the slight blow upon her bare arm, but she was unable to perceive the snake, in spite of somewhat careful search for it. Being accustomed to be circumspect about dangerous reptiles almost all her life, she had examined the ground well before approaching the jessamine tree; but she had been less careful in her inspection of the tree itself, because she believed that poisonous snakes were unlikely to be found in trees.

If the snake were a moccasin (Ankistrodon piscivorus)—as seems to be most probable—almost anyone in the least off-guard would have failed to have seen it, just as she did; for its white buccal surfaces would have been turned straight toward her, and they would readily have been taken for jessamine blossoms. Some of the symptoms suggest also that this was the species of snake concerned; for example, the pain was accompanied throughout with numbness; there was no ecchymosis, but puffiness about the fang-punctures appeared immediately; and swelling, involving the upper two-thirds of the affected forearm and extending almost entirely around it, had developed within one-half hour when I saw her.

I found this forearm was one inch (25 mm.) larger in circumference at its largest part than the other. (I ascertained afterward that in health both forearms were of the same size.) It was almost entirely anesthetic. Some part of each of these manifestations must

have been due to a ligature that had been applied snugly above the elbow of the bitten arm, but it was not tight enough to suppress the radial pulse, which was 80 per minute. Attention to the anesthesia was accentuated when her husband cut her skin slightly while removing the ligature about one-half hour after I had injected 12 c.c. of antivenin (Calmette's *sérum antivénimeux*) subcutaneously in three doses at points a short distance around the fang-marks; she did not know it until he told her.

These fang-wounds showed plainly, and each had bled a large drop or more, and bleeding continued slightly after turpentine—a good styptic—and kerosene had been applied. I explored each puncture with a big sewing-needle after having injected the antitoxin, as described above, and I found that the one on her forearm's outer aspect, which had been made by the snake's left fang, had penetrated the integuments of this region, and that the other had gone well into the derma, but in a direction downward toward the hand. No other marks were observed on the forearm. They were less than three-eighths of an inch (9 mm.) apart, which proves the small size of the snake and shows it to have been a viperine one.

I do not think that the other symptoms observed are noteworthy, especially as she had partaken liberally of whisky—about a pint, she thought. She was prepared to add corroboration to the current popular belief that victims of poisonous snakes cannot be intoxicated, but I prefer to reject this testimony along with all of her subjective symptoms.

With the understanding that it be received for what it may be worth, I shall add that she said that the pain rapidly diminished and soon disappeared altogether after the injection of serum. I left with her relatives the remainder of the *flaçon* to be used, if required by symptoms arising later; but it was not administered. The next day there was a patch of dense infiltration as large as a man's palm around the bite and the swelling had not abated notably. It disappeared altogether in a week. For three days its brawniness was notable. The fang wounds healed perfectly without scarring by the process of scabbing.

Owing to the evident small size of the snake concerned with this case, and the almost necessarily small dose of venom that it inserted, it is improper to claim here anything more than that antivenin appears to neutralize in human beings to some extent, as Calmette has claimed, viperine venoms. This fact is entitled to some consideration, I think, in view of the undoubted efficacy of antivenin in the treatment of the attendant bitten last summer in the Washington Zoölogical Gardens by a large Florida diamond-backed rattlesnake. I think also that its potency in removing symptoms of neurotoxic absorption in a case of rattlesnake bite that I have reported[1] deserves

[1] American Medicine, September, 1906, 310.

to be borne in mind, especially in connection with Prentiss Wilson's[2] academic deductions, that the antitoxin treatment of the bites of indigenous venomous serpents is impracticable.

It can, I think, be shown that the deaths from bites of venomous snakes in certain of our Southern States approach in numbers those caused there by lightning; and I feel sure that many of the former are quite readily preventable, if Calmette's, Noguchi's, and other work—now neglected—be applied as it has been applied in Japan, for instance, and that, too, in connection with a viper.

SOLITARY TUBERCULOSIS OF THE BREAST.

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Tuberculous disease of the breast is apparently very exceptionally met with in hospital practice. Indeed, until comparatively recent years there is scant mention of the condition in English literature, the bulk of the cases reported being those of French and German observers. With the one exception of Sir Astley Cooper, to whom is due the honor of having first, in 1829, in his "Illustrations of the Diseases of the Breast," described clearly under the term "Scrofulous Swellings" cases belonging to this category, there is no report in English literature of the observance of the condition prior to 1888;[1] this, too, in spite of exhaustive treatises upon the subject by Klotz[2] in 1879, by Richet[3] in 1880, Dubar[4] in 1881, Ohnacher[5] in 1882, Orthmann[6] in 1885, and many other extensive monographs and text references within the next five or six years by well-known Continental clinicians. And, even subsequent to the review of Shattock,[7] in 1889, the condition remained unrecognized, or, at all events, was not reported, in the large English clinics for some time.

Since the establishment by Dubar,[8] in 1881, of the diagnosis of this condition upon a histological and bacteriological basis, and its recognition as a clinical entity, there have been in all about forty cases reported, which conform to the term "Solitary Tuberculosis of the Breast." This term, suggested by Geissler[9] to cover those cases in

[2] Archives of Internal Medicine, June, 1908.
[1] Transactions of the Pathological Society, London, 1888, xxxix, 446.
[2] Arch f. klin. Chir., 1879, Band xxv.
[3] Gaz. des hôp., 1880.
[4] Des tubercules de la mamelle, Thèse de Paris, 1881.
[5] Arch. f. klin. Chir., 1882, Band xxviii.
[6] Virchow's Archiv, 1885, c, 365.
[7] Trans. Path. Soc., London, xl, 391.
[8] Loc. cit.
[9] Deut. med. Woch., 1906, xliv, 1780.

which the breast only was found to be diseased, excludes not only those giving a history or evidence of earlier tuberculous disease elsewhere, but also those in which the breast condition might be considered secondary to existing disease of the lungs, joints, etc., or as a direct extension from infected axillary lymph nodes.

While no case of primary tuberculosis of the breast has been confirmed by autopsy, solitary tuberculous infections of the genital tract do occur in women (such as the fifteen cases accepted by Veit[10]). It is, therefore, a reasonable presumption that such lesions may also be met with in the breast.

It has been a matter of no small difficulty to reach a satisfactory estimate of the number of reported cases of tuberculosis of the breast which conform to the term "primary" or "solitary." Only those cases have been included in this series in which careful search has failed to detect evidence of tuberculosis elsewhere. This is the only reasonable or possible ground upon which a classification can be based, in view of the total absence of autopsy records.

PATHOGENESIS. It is somewhat difficult to dogmatize upon the exact method of infection of the mammary gland, but if we adhere to the limitations of the term solitary mammary tuberculosis as defined above, we are restricted to the consideration of the three following as the most common: (1) Indirect—hematogenous; (2) direct—(*a*) through the lactiferous ducts and their lymphatics; and (*b*) through wounds, fissures, or abrasions (cutaneous lymphatics).

PREDISPOSING CAUSES. *Age.* There is no reported case before puberty, while the number decreases rapidly after the menopause, the most advanced age recorded being fifty-three years, a case observed by Remy and Noel.[11] Thus the period of reproductive activity embraces the vast majority of these cases.

Lactation. In addition to the maturity of the gland, lactation would seem to be a predisposing factor, possibly the most important, as the incidence of the disease in married and unmarried subjects has been in the proportion of 4 to 1. No doubt the susceptibility to infection during gestation and lactation is analogous to that recognized in pulmonary disease, in which infection or recrudescence is, unhappily, a frequent sequel of childbed.

Inflammation. In those cases occurring in glands which have functionated, there is a history of inflammation complicating lactation in 42 per cent., and suppuration in 20 per cent.

Traumatism as a predisposing factor has rarely been mentioned, although noted by Poirier,[12] and Sabrazès and Binaud.[13]

CLINICAL FORMS. Two clinical forms of the disease are generally recognized: (1) nodular—discrete—disseminated nodular; and (2) confluent.

[10] American Gynecology, September, 1903.
[11] Bull. de la soc. anat. de Paris, 1893, p. 412.
[12] Contrib. à l'etude des tumeurs du sein chez l'homme, Thèse de Paris, 1883.
[13] Arch. gén. de méd., 1896; Arch. de méd. expér., 1894, p. 838.

In the *nodular form* of the disease, one or more nodules are found, generally deeply embedded in the parenchyma of the gland. The disease tends to run a protracted course, the nodules frequently remaining the same size for years; eventually they gradually increase in size and proceed through the stages of degeneration, suppuration, and fistula formation. In a case reported by Scudder,[14] the condition ran a course of five years, and in a case of Mandry,[15] four years. Such a prolonged course is, however, exceptional, caseation and disintegration occurring, as a rule, within a year from the onset. Not infrequently, nodules coalesce, forming abscesses of considerable size. As might be expected in the nodular form of the disease, running as it does a chronic course, the onset is extremely insidious. Pain is generally absent in the earlier stages, and the breast may remain for some time unchanged in appearance. When foci occupy the central zone and the walls of one or more ducts are involved in the connective tissue changes, retraction of the nipple gradually develops.

In the *confluent form*, the onset is more acute; there is greater enlargement of the breast, pain is an early symptom, and degenerative changes, with fistula formation, develop early. It is this form of the disease which is most frequently met with during lactation; in the majority of cases it is centralized beneath the ampulla, suggesting an infection through the lactiferous ducts.

In all cases the breast is freely movable upon the pectoral muscle, and fixation of the skin over the foci develops only with their degeneration. Rarely more than one gland is involved, even when the disease is extensive and fistulas have existed for some time.

In both forms of the disease the axillary glands in the majority of cases are involved to a greater or less extent, the process being either tuberculous (75 per cent.) or simple hyperplastic adenitis. Where the primary lesion has existed as a solitary nodule in the upper and outer quadrant, running a chronic course, the secondary infection of the axillary lymph nodes may so outstrip the primary focus as to give rise to the belief that the glands themselves were the starting point of the disease. This fact has proved a point of difficulty in classifying the reported cases. While the direction of the lymph stream would suggest that the lymph glandular involvement, in the majority of cases, follows the breast infection, the frequency with which disease of the breast has been noted in the outer quadrants suggests the possibility of a retrograde infection, quite apart from those cases in which the process in the lymph nodes and breast can be shown to be contiguous.

Atypical Clinical Forms. Atypical clinical forms of solitary tuberculosis of the breast have been met with. Roux[16] describes a form

[14] Amer. Jour. Med. Sci., 1898, cxvi, 75. [15] Beit. z. klin. Chir., 1891, viii, 179.
[16] De la tuberculose mammaire, Thèse de Genève, 1891.

of intraglandular cold abscess, considered by Schley[17] as a terminal product, usually of the confluent type. It is of slow development and associated with diminution in the size of the breast. Orthmann[18] reports a case in which the disease apparently began as a subcutaneous infection, resembling an ordinary furuncle, with subsequent induration and extension of its base, resulting ultimately in the formation of a tumor of considerable size. Poirier describes a case in which two small cutaneous vesicles developed into indurated tuberculous masses. In the case of Kramer,[19] a primary lesion was noted, in the form of an ulcer, near the nipple, followed by the development of nodules within the breast, connected with the ulcer by bands of indurated tissue. In Demme's[20] case, tuberculous infection was ingrafted upon the margin of a pre-formed sinus, the result of a pyogenic mastitis. Finally, there is the case of Pluyette,[21] frequently cited, that of an unmarried woman, aged twenty-three years, in whom a swelling of the breast followed within a few days a slight wound of the nipple, and proceeded to suppuration. Tubercle bacilli were found in the nodule beneath the areola.

Retraction of the nipple has been noted as a primary symptom in three cases: in the case of Dubreuil,[22] retraction occurred two years before the observation of a tumor; in the case of Verneuil,[23] it was noted after confinement five years before the detection of an intraglandular mass. Warden[24] also reports a case in which a patient following her third gestation observed retraction of the nipple, whereas the glandular tumor only became manifest twenty-one months later.

It should be noted that the course of the disease in the confluent form is not infrequently hastened by the presence of a secondary (pyogenic) infection, and to this category belongs that group of cases running a rapid course and diagnosticated as simple pyogenic mastitis, which, after incision and drainage fail to heal, with the final development of widespread tuberculous infiltration and the persistence of multiple sinuses.

Pathological Anatomy. The pathological picture of tuberculous disease of the breast presents no striking differences from that of tuberculous processes elsewhere. While the degree and extent of the inflammation surrounding the nodule or nodules vary, there is always the classical picture of peripheral infiltration with lymphoid and plasma and more centrally epithelioid and giant cell formation, and a central zone of degeneration showing defective chromatic staining or actual caseation. In advanced nodular or acute confluent cases there is, of course, abscess formation, the pus sometimes

[17] Annals of Surgery, 1903, xxxvii, 510.
[18] Virchow's Archiv, 1885, c, 365.
[19] Cntrlbl. f. Chir., 1888, p. 867.
[20] Schmidt's Jahrbuch, 1891.
[21] Gaz. heb. de méd. et de chir., 1900, No. 103.
[22] Gaz. méd., Paris, 1888; Gaz. heb. des sci. méd., 1890.
[23] Prog. méd., 1882.
[24] Medical Record, 1898, liv, 479.

containing, as in my case, numerous polymorphonuclear leukocytes, in addition to tissue detritus. The walls of the abscess cavities usually contain numerous secondary tubercles varying in size from a millet seed to a pea, in various stages of growth and degeneration.

In all cases included in this series the diagnosis was confirmed either by histological or bacteriological examination or by animal inoculation. The case which I have to record is the first reported instance in which tubercle bacilli in pure culture have been grown primarily from the lesion in the breast.

DIAGNOSIS. In view of the fact that the majority of cases of solitary tuberculosis of the breast have been noted in individuals of robust health, the diagnosis, especially of the discrete or nodular form, presents innumerable difficulties. When the tumor has been deep seated and retraction of the nipple present, without inflammatory signs in the axillary nodes, the clinical diagnosis of carcinoma has invariably been made. Happily, as the most approved local treatment (that is, wide and complete removal of diseased tissue), is the same in both conditions, no harm can have resulted; but, in view of the growing conservatism in the treatment of localized tuberculous infections, and the substitution of tuberculin therapy for radical operation in selected cases, it is possible that in the future one may consider operation inadvisable, especially in cases in which the possibility of lactation can be excluded. In such cases, the importance of differentiation is apparent, and may be achieved through the administration of sufficient tuberculin to produce a local reaction. When the latter occurs, one can be satisfied that the mass is not carcinomatous, although exceptions may be possible, the co-existence of carcinoma and tuberculosis having been reported by Pilliet and Piatot,[25] and Warthin.[26] In cases in which the gland is active, careful search should be made for tubercle bacilli, and animal inoculation should be carried out.

From acute pyogenic mastitis, tuberculous disease may, as a rule, be differentiated by its more chronic course, exceptional cases being those, as before stated, in which the two infections co-exist. From simple cysts tuberculous disease may be readily differentiated, the former being more regular in outline, elastic, painless, and without adenitis. Aspiration may be practised in confirmation. Fibromas and fibro-adenomas present greater difficulties. They are, however, free from inflammatory signs or evidence of lymphatic involvement. The pure fibromas, especially, are distinctly movable within the gland, and neither react to tuberculin, although, in a case reported by Davis,[27] tuberculous disease was found engrafted upon a pre-existing adenomatous tumor. In sarcoma the disease may

[25] Bull. soc. anat. de Paris, 1897, p. 424.
[26] AMER. JOUR. MED. SCI., 1899, cxviii, 25.
[27] Medical News, 1897.

remain stationary and encapsulated for a prolonged period, followed by rapid growth unassociated with inflammatory symptoms, early involvement of the skin, and enlargement and engorgement of the cutaneous veins. Gummatous tumors are usually to be differentiated by the history, the presence of other lesions, or response to antiluetic treatment. In chronic mastitis, the process is diffuse. There is an absence of lymphatic infiltration and of a definite mass. Here, too, in doubtful cases the use of tuberculin may lead to a satisfactory differentiation. Actinomycosis of the breast is extremely rare, only five or six cases having been reported. In the earlier stages, differentiation from tuberculosis without local reaction from tuberculin is probably impossible; once sinuses are formed, however, the nature of the discharge in cases of actinomycosis at once gives a clue to the diagnosis.

TREATMENT. The treatment of this affection may be considered under the headings of (1) local, and (2) general.

Local. While it is conceivable that a partial extirpation might be the rational practice in cases in which a single nodule has developed in the periphery of the gland without lymphatic infection, it is the consensus of opinion that complete amputation of the breast should be carried out in all cases, together with the resection of the axillary glands when these are thought to be the seat of tuberculous disease. From a somewhat extensive experience in the treatment of localized tuberculous infections, with the aid of tuberculin as an adjuvant to general hygienic and dietetic measures, I am forced to the opinion, however, that under specific conditions one may be justified in staying operative interference until the effect of a course of tuberculin has been ascertained. Such cases may be considered favorable for this plan of treatment in which the disease is discrete, when chronicity is a prominent clinical feature, and when the possibility of lactation can be safely excluded. This latter point is of the utmost importance, as will be shown subsequently, but I think it may be here stated, without ground for contradiction, that a breast the seat of chronic tuberculous disease, altered anatomically by the development of scar tissue, and especially one in which there is retraction of the nipple, should not be allowed to functionate.

General. Though one may be reasonably sure that the breast infection is of the solitary type, there can be no certainty that infection of the viscera, joints, etc., may not subsequently develop, even in those subjects in whom total extirpation of the palpable disease has been practised. It is, therefore, of the greatest consequence that, not only in those cases in which operative interference is held in reserve, but also in those in which the local treatment has been radical, some plan of general treatment should be followed, as those operated upon may still remain susceptible to re-infection, and the non-operative cases to the development of metastases. To this end both classes of patients should be urged to effect a radical change in

the environment in which the disease was contracted. If an actual change of location is beyond the means of the individual, she should be relieved of all household work and the innumerable exactions upon time and energy which the direction of a household and its affairs entail. For a period of at least three months, absolute rest should be insisted upon. The greater part of each day and every night should be spent in the open air, the benign effects of fresh air being quite as important in the treatment of surgical infections as in pulmonary disease. One should not be satisfied with any proposed substitute. However liberal room ventilation may be, it should be recognized that "outside air" cannot be imported.

In addition to three meals of properly cooked and nutritious food —including rare meat and green vegetables at least once a day— milk and fresh eggs should be taken between breakfast and the mid-day meal, during the afternoon, and before retiring. If eggs are too costly, or are unobtainable owing to the season, milk alone may be taken, beginning with one quart a day in addition to that taken at mealtime.

Further, the patient should be instructed to keep an accurate record of the hours spent each day in the open air, the quantity and nature of food taken, together with the weekly gain in weight. These records should be scanned by the surgeon at each return of the patient for inoculation.

Finally, tuberculin in some form should be administered regularly. It is important that constitutional symptoms should not follow such inoculations, as, in the event of the development of a hypersensibility to tuberculin, its discontinuance might be necessary for some months. Inoculations should be repeated at intervals of ten days to two weeks, extending over a period of one year. If T. R. (tuberculin) be employed, the initial dose to an individual of average weight should not exceed $\frac{1}{1500}$ milligram. The value of increasing the dosage to more than $\frac{1}{1200}$ to $\frac{1}{1000}$ milligram is doubtful. Under no conditions should the increased dosage be permitted when injections are followed by constitutional symptoms, such as headache, malaise, or fever.

I think it is now generally accepted that in the treatment of localized tuberculous infections the use of tuberculin in some form, as an adjuvant to the measures above enumerated, yields results which are unobtainable when the exhibition of this agent is withheld. The bacillary product recently invented by Professor Vaughan, of Ann Arbor, containing, as it is thought, only the non-poisonous elements of cultures of the tubercle bacillus, has yielded excellent results in the treatment of localized infections, and its further exploitation may prove that we have in it an agent which may be administered in increasing amounts, without risking the serious danger of a prolonged hypersusceptibility or "negative phase."

PROPHYLAXIS. I feel that a review of this subject would be lacking in force and deprived of one of its most important aspects if the question of the infectivity of the milk of tuberculous subjects were not briefly touched upon. Our knowledge of the comparative pathology of mammary tuberculosis conveys such a forceful lesson that even if we were without definite cognizance of cases of transmission of the disease from mother to child we should feel compelled in all cases of mastitis during lactation to consider seriously the possibility of the existence of a tuberculous infection. There are, however, cases described in which the evidence of direct transmission is most startling. The first in English literature, that observed and reported by Hebb in 1888, is a striking instance of the danger to the offspring, five out of eight children having died of tuberculosis. It should be stated, however, that this woman, in addition to mammary disease, had been treated for some years for pulmonary tuberculosis.

While bacteriological observations upon the secretion of glands known to be tuberculous have been scanty, women with tuberculous breasts have been seen nursing tuberculous infants.

PROGNOSIS. Material on which to base an opinion as to the prognosis in solitary tuberculosis of the breast is, unfortunately, very scanty, owing, no doubt, to the difficulty experienced in inducing patients to return from time to time for examination after they have been discharged well. If an analogy to other forms of localized tuberculosis in otherwise healthy individuals may be invoked, the prognosis should certainly be favorable. We are, however, in possession of a record of after-examinations, chiefly upon patients treated surgically in the Tübingen clinic, and reported by Braendle[28] in June, 1906. This author's table embraces the after-histories of fifteen cases which may be accepted as primary infections. Of these 15, two died several years after operation from phthisis without evidence of local recurrence. Of the remaining 13, none had shown local recurrences or evidence of disease elsewhere, although several had been operated on four, eight, and eleven years previously; two patients remaining free from the disease sixteen and nineteen years after operation. Further, of these 13 living patients, 10 were either at the end of the fortieth or the beginning of the fiftieth year at the date of last examination. It is the opinion of Braendle that, in comparison with tuberculosis of other organs, primary tuberculosis of the breast may be considered a less unfavorable affection.

CASE REPORT.—K. M., aged twenty-four years, single, dietitian. Complains of pain and swelling in the right breast.

The *family history* was negative.

Personal History. She had pneumonia at seventeen, with an uneventful recovery. In the spring of 1904 a nodule developed in

[28] Beit. z. klin. Chir., 1906, Band l.

the right breast at the site of the present swelling, which gradually increased in size, burst at the end of three months, and continued to discharge for a further period of four months. The condition was diagnosticated at the time as "cold abscess." Since 1904 the patient has remained well.

Present Illness. On March 20, 1908, the patient first noticed pain and the presence of a swelling below and to the outer side of the right nipple.

Present Condition (March 27, 1908). The patient is fairly well nourished and looks healthy. Mucous membranes are of good color. The left breast shows no enlargement or diminution compared with the right. Below and to the outer side of the right nipple, at the margin of the areola, there is a swelling the size of a pigeon's egg over which the skin is of a bluish gray color. The nipple shows a moderate grade of retraction. On palpation the whole breast appears to be firmer than normal, is freely movable upon the pectoral fascia, and is without evidence of localized disease except at and about the site of the aforementioned swelling, which is found to consist of a central portion, tense and fluctuating, surrounded by an area of infiltration adherent to the skin and shading off gradually into the surrounding gland tissue. Tenderness is not a marked feature, and there is no redness of the cuticle nor local increase of temperature. The nipple cannot be withdrawn. In the right axilla there is a soft palpable gland the size of a bean. Examination of the thoracic and abdominal organs is negative. There is no enlargement of the superficial lymphatic glands apart from that mentioned in the right axilla. Urine analysis is negative. Temperature is 98.2° at 4 P.M.

March 30. There has been a slight increase in the size of the fluctuating area since last seen. Under aseptic precautions the abscess was evacuated and 2 c.c. of viscid grayish pus withdrawn. Cultures on serum and hemoglobin-agar after twenty-four hours are negative. Smear preparations show numerous polymorphonuclear leukocytes, but no bacteria. A portion of pus was also inoculated subcutaneously into a guinea-pig.

March 31. At 4 P.M., tuberculo-ophthalmic inoculation (1 per cent.) was given.

April 1. At 9 A.M. no reaction was present.

April 4. Under ether anesthesia, amputation of the right breast was performed without opening the axilla. Convalescence was uneventful.

PATHOLOGICAL REPORT. *Macroscopically*, on cross-section the body of the gland looks like sarcomatous tissue, the cut surfaces having a glairy appearance, evidently due to a diffuse fibrosis. Below and to the outer side of the nipple the skin is adherent over a small abscess cavity which contains grayish mucoid pus. The walls of the cavity are irregular and villous in appearance, and of a

dirty gray brown color. Surrounding the abscess cavity is a dense area of acute inflammatory infiltration the size of an English walnut. Only one caseous area the size of a pea was found, the contents of which were transferred to slants of modified Dorset egg medium.

Microscopically, smear preparations show innumerable polymorphonuclear leukocytes; no bacteria. Stained sections from the wall of the abscess cavity show numerous recent tubercles with epithelioid and giant cells as well as central necrosis. Dr. Duval thinks it probable that the bacillus was of the bovine type, owing to the rapid course of the disease, the large number of polymorphonuclear leukocytes present in the pus, and the acute nature of the process histologically. The culture, however, was lost before titration observations could be carried out. The difficulty in maintaining the growth upon artificial media is an additional point in favor of a bovine infection.

After-treatment. Since operation, the patient has followed in a general way the line of treatment suggested in the body of this paper. Injections of T. R. (tuberculin), $\frac{1}{1500}$ milligram, have been administered every ten days. When last seen, in October, 1908, the patient was in excellent condition, and reported a gain in weight of eighteen pounds.

TUBERCULOUS PULMONARY CAVITIES IN INFANTS.

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The presentation of this paper on cavity formation in tuberculosis of the lungs in infants under two years of age has for its object, first, to record six cases; and second, to call attention to the frequency and location of pulmonary cavities at this age. In reviewing the literature the fact impresses itself that many writers on diseases of infants treat the subject in a very indefinite manner. Some do not refer to it, while others speak of it as if tuberculous cavities in infants followed the general course of events so frequently seen in the adult. This is somewhat surprising, because most of the authors who have written especially on this subject point out how difficult it is to make an antemortem diagnosis of a cavity in comparison to the condition in later life. We have had difficulty in selecting our cases from the literature, because many authors have failed to make the distinction between infancy and childhood. For our purpose, the subject may be divided into the following heads:

(1) The frequency of cavity formation in the lungs of infants; (2) the pathology of the condition; (3) the location of the cavities in the lungs; and (4) the report of six cases.

1. The Frequency of Cavity Formation in the Lungs of Infants. From the literature, we have been able to find special mention of cavity formation in quite a number of instances. These cases have been sifted from general discussions of the subject, rather than special reports of cases. We believe many cases have not been recorded because observers have not deemed it of sufficient importance to report them. Clinically, in the vast majority of cases cavity formation in the lungs of infants is entirely overlooked. We believe, therefore, that by calling attention to its frequency and localization, cavities should be more often recognized during life.

Leroux, in analyzing Parrot's cases, found cavity formation present in 57 cases out of 219 autopsies on patients under three years of age; that is 26 per cent. of the cases. He particularly mentions 5 of these cases which were under three months of age, but unfortunately no reference is made of the number under two years.

Warthin and Cowie quote Hugunin as reporting 2 cases, a seven-month premature infant and an infant seven weeks old; Berti, 1 case nine days old; Demme, 1 case eleven weeks old; Queyrat, 1 case three months old; and Flesch, 8 cases out of 500 autopsies on children in the early months of life. Demme reports 1 case, aged four weeks; F. Weber, 1 case, aged three months; Henock, 5 cases, aged four, seven, eight, ten, and eighteen months; Comby, 4 cases, aged four, six, eight, and nine months; and Deliarde, 1 case, aged six months, and speaks of the rareness of cavity at this age. Symes and Fisher, in reporting 500 deaths at various ages from tuberculosis, refer to two cases with cavities at five and eight months of age. Shennan reports 23 cases out of 355 cases (6.5 per cent.). Carmichael reports 2 cases, aged eight and fifteen months; Toulmin, 1 case, four months old; Donkin, 1 case, aged 1 year; Fry and Shaw, 1 case, twelve months old; Price-Jones, 3 infants, thirteen, sixteen, and twenty-two months old; J. Lewis Smith, 1 case, aged seventeen months; Green, 6 cases under two years; and Barthez and Sanne report 10 cases under two years.

Zuber says, "All authors agree that cavities are rarer in children than in adults." Baginski states: "Chronic tuberculosis with cavity formation in young children in characteristic form, as in the adult, is an infrequent disease." Other authors, as Rotch, Monti, Jacobi, Still, Osler, and Ashby, speak in general terms of the rarity of cavities in infants under two years compared with older children. The above mentioned cases, in all likelihood, do not represent the observations of these men as to the frequency of cavity formation, but simply some of the cases which they have had occasion to refer

to in reports. On the other hand, the following observers have found cavitation in infancy of more frequent occurrence: Northrup, in a personal communication, says: "Tuberculous cavities are not rare in infants as young as a few weeks even. They follow the law which would seem to apply to adults. The lesion is common." Rilliet and Barthez report cavities in the proportion of one to three, in cases from one to two and one-half years. Holt says, "Areas large enough to deserve the name cavities were present in 35 of 72 autopsies upon tuberculous patients, two years and under." De Rothchild states that pulmonary cavities are observed in one-third of the cases from one to two and one-half years. Hervieux reports that one-fifth of the cases in the course of the first year of life have pulmonary cavities. J. Francis Condie even went so far as to say, "Tuberculous cavities are much more frequent in very young children than in adults." Warthin and Cowie quote Weber as making the statement that he had many times observed tuberculous cavities of the size of half a lobe in children under the age of three months.

From the above resume of the literature, it will be seen that cavity formation in infancy has been observed by some observers in a high percentage of cases, while by others it has been found but rarely. From the comparatively few cases which we have been able to collect from the literature, the earliest case occurred in an infant premature at the seventh month, while the majority were found beyond the third month, with increasing frequency toward the end of infancy.

In order to study the frequency of tuberculous cavities in infants at the Children's Hospital of Philadelphia, the records for the past sixteen and three-quarters years have been reviewed. We have found that during this time 4518 infants have been admitted to the wards of the Hospital. Of this number, 1140 infants have died. The number of autopsies performed was 371, of which 75 disclosed tuberculosis. Of the total number of deaths, 6.5 per cent. were tuberculous. However, these figures are only approximate, because only one-third of the children dead were autopsied. Again, when we compare the number of tuberculous autopsies with the total number of admissions during this period, it will be found that 1.6 per cent. were tuberculous.

It will be seen from these statistics of the autopsy records that with us tuberculosis in infants under two years of age is an infrequent disease. This can partly be explained by the fact that the great number of infants coming to the hospital have some form of advanced gastro-intestinal disorder. If the actual number of cases of gastro-intestinal disease be studied from our autopsy reports, it will be seen that 155 of the 371 autopsies, or 41.7 per cent., were grouped under this head. Therefore, if these cases of advanced gastro-intestinal disease be omitted from our comparison, it will be seen that of the remaining autopsies (216) there were 75

cases, or 34.5 per cent. tuberculous. This latter comparison really emphasizes the high mortality of gastro-intestinal disorders (41.7 per cent.) far more than it does that of tuberculosis (34.7 per cent.) at this age. We believe, from the clinical aspect at least, that our former percentage of 1.6 per cent. of fatal cases is nearer the truth as far as tuberculosis at this age is concerned.

Below we have tabulated the ages of the tuberculous autopsies on infants:

First Year.	Cases.	*Second Year.*	Cases.
1 month old	0	12 months old	7
2 months old	1	13 " "	3
3 " "	2	14 " "	6
4 " "	1	15 " "	4
5 " "	5	16 " "	3
6 " "	9	17 " "	3
7 " "	5	18 " "	6
8 " "	3	19 " "	4
9 " "	2	20 " "	1
10 " "	5	21 " "	1
11 " "	2	22 " "	0
		23 " "	2
	35		40

Number of tuberculous autopsies on infants under one year, 35.
Number of tuberculous autopsies on infants between one and two years, 40.
Total number of tuberculous autopsies on infants under two years, 75.

To study the frequency of cavity formation in the lungs of infants dead of tuberculosis, we have gone over the records of the Children's Hospital, and found that cavity formations were present in 12 of the 75 subjects dead of tuberculosis (16 per cent.).

As we stated above, we encountered difficulty in trying to estimate this frequency from the literature. In only a few reports were actual statements as to percentages obtainable: Holt reported cavity formation in the proportion of 1 to 2; Rilliet and Barthez, and De Rothchild, in the proportion of 1 to 3 (these cases were one to two and one-half years old); Hervieux, 1 to 5 (during the first year of life). In our cases 1 in 6 showed excavations, which is a considerably lower percentage than the observations of the above authors. Nevertheless, it will be seen, even in our cases, that cavity formation at the autopsy table is not uncommon.

If we consider the frequency of this process in older children, as compared to our findings in infants, it will be seen that in the former cavitation is not only more frequent, but follows the rule applying to adults. The usual explanation of this condition is conceded to be the greater resistance offered as the child grows older, allowing the process to become of a more chronic nature, and thus giving mixed infections greater opportunity to act.

Table Showing the Ages of the Cases Under Two Years of Age with Tuberculous Cavities at the Children's Hospital.

5 months old	1
6 " "	4
7 " "	1
11 " "	1
12 " "	1
15 " "	2
17 " "	1
19 " "	1
Total	12

II. The Pathology of the Condition. In considering the pathology of tuberculosis at this age, a brief resume of the types of lesions may be of some value. It is not our purpose, however, to consider in detail these various lesions. Briefly the general pathology of tuberculosis at this age may be divided into three types: (*a*) Acute miliary tuberculosis; (*b*) chronic tuberculosis with fibrous changes; and (*c*) bronchocaseous pneumonic tuberculosis.

(*a*) *Acute miliary tuberculosis,* or acute disseminated miliary tuberculosis, of the lungs is considered rare by the majority of authors at this early age of life. When it does occur the miliary tubercles, either gray or yellowish gray in color, are found scattered throughout both lungs, and to a less extent in other organs of the body. These tubercles vary in size and number according to the degree of infection and the duration of the disease.

(*b*) *Chronic tuberculosis with fibrous changes* in the lungs can be very briefly considered here, because it scarcely enters into the discussion of our paper from the fact that many of the changes in the tissues are of a chronic nature. This type of tuberculosis at first is generally localized to a small area or areas, and the process is accompanied by the production of fibrous tissue. The process may consist of caseating areas containing small cavity formations, surrounded by more or less fibrous tissue. Distinct chronic tuberculosis of the lungs with cavity formation within the first two years of life, compared to the adult type of the disease, is rarely found at autopsy.

(*c*) *The caseous bronchopneumonic* type of tuberculosis is the most frequent form of the disease in the lungs at this age. It runs a more or less subacute course, and is almost always fatal. The advanced caseous lesions are usually confined to one lobe, or to one lung, with less marked lesions in the other lobes or lung. In a section of a lung, showing tuberculous lesions of this type, there are usually large caseous areas with intervening areas of bronchopneumonia, congested lung tissue, or normal lung tissue. The multiple lesions so frequently seen in these cases have their origin from some older process and are disseminated by way of the blood, lymphatics, or by insufflation. They increase in size from peripheral extension, and by the fusing of closely situated smaller areas. This method of

extension is especially to be seen when the lesions are near the opposing surfaces of the lobes and it is not uncommon to see the greater part of one lobe with the adjacent parts of another lobe, involved in the caseous process. The interlobar pleura in such cases is obliterated by the tuberculous process, or stands out prominently as a fibrous band stretched across the caseous area. It is in these large caseous areas that cavity formation most frequently begins at this age. Cavities are usually the result of acute softening of the central parts of the caseous mass, and when this softened area communicates with a bronchus the fluid parts are thrown off, leaving a space or cavity. The softening of the caseous mass is generally the result of secondary infection, and is usually due to Streptococcus pyogenes, Staphylococcus pyogenes aureus and albus, Micrococcus tetragenous, or Diplococcus pneumoniæ. A pure tuberculous process, as a rule, does not tend to liquefy, it being a dryer, harder, and more cheesy process. This in itself would explain the infrequent cavity formation in our group of cases.

In examining the lungs of this type of tuberculosis one frequently finds small softened areas in these caseous lesions. These have been recorded by authors as instances of cavities; they in all likelihood would produce cavities in the course of time. We have not included such areas as cavities in our cases, because as antemortem excavations they had not existed.

The walls of the cavities are usually irregular in outline and somewhat darker in color than the surrounding lung tissue; especially is this true if the cavity has existed for any length of time. A distinct communication with a bronchus may be found on some part of the cavity wall; it may, however, be small and difficult to locate. The size of the cavity varies usually with the chronicity of the case and the size of the caseous lesion. From the microscopic examination of these cases it would seem that the process is rapid, as the walls of the cavity consist almost entirely of caseous material. Fibrous tissue formation in the walls of the cavities does not take place to any great degree in this group of cases, compared to the formation of this tissue in the adult.

The fact that in early infancy the tuberculous process in the lung is generally of an extensive bronchocaseous type, running an acute or subacute course, explains to a certain extent the absence of fibrous tissue in the lesions. It is a fact that the younger the individual, the more extensive the involvement and the more acute the course. This statement is the result of autopsy examinations, and does not take into consideration the numerous infections with the tubercle bacillus which undoubtedly occur in early life, and are held in abeyance or cured. As many of these latter cases are not diagnosticated, the occurrence of the disease can only be surmised from the widespread prevalence of tuberculosis. It is only in the susceptible cases at this age that the process becomes diffuse and of an acute or sub-

acute course, ending fatally. It may also be noted here that in infants dying of tuberculosis, the lungs are involved in 100 per cent. of the cases.

III. The Location of the Cavity. The literature on the subject of the localization of the cavity is not very extensive. The majority of authors state that cavity formation usually takes place in the lower lobes, and generally at the root or central part of the lung. Thus, D. Francis Condie says: "There is an important modification that should guide the practitioner when he seeks to determine the existence of a cavern in young children, viz., that under five years of age, the cavernous excavation is generally seated in the lower or middle lobes, and is almost always confined to one side of the chest." James M. Coley found cavities in infants much more frequently in the inferior lobes, and most often on the right side. Zuber also found the right lung most commonly affected, and generally only one lung. Again, both J. Walter Carr and S. Vere Pearson have observed that in infants the usual location of cavities is at the root or central portion of the lobe. Berti and Demme each report cases with a cavity in the lower lobe of the right lung. Fry and Shaw report a case with a cavity in the lower lobe of the left lung. Price-Jones reported an infant with cavities in the same location; but report another case with a cavity in the upper lobe of the left lung. Hugunin reported an infant with a cavity in the apex of the left lung. Henock reported four cases:

An infant, four months old, right upper lobe, two cavities.
An infant, seven months old, right upper lobe, two cavities.
An infant, four months old, right upper lobe, two cavities.
An infant, eighteen months old, both lungs, numerous small cavities.

J. Lewis Smith reported one case at seventeen months, with cavities in both upper lobes. P. Bennis Green reported 6 cases as follows:

An infant, two years old, summit of right lung.
An infant, two years old, middle lobe of right lung.
An infant, two years old, upper lobe of left lung.
Three infants, two years old, lower lobe of left lung.

On the other hand, Eustace Smith says, "The masses situated nearest the apex are commonly the earliest to liquefy, but not always."

Barthez and Sanne, in 77 cases of cavity formation in infants, found:

Cavities within the right lung, 47.	
Right upper lobe	34
Right middle lobe	9
Right lower lobe	16
Cavities within the left lung, 51.	
Left upper lobe	51
Left lower lobe	18

The location of the cavities in the cases at the Children's Hospital may be tabulated as follows:

Left lung, 6.	
Left lung, upper lobe	2
Left lung, anomalous middle lobe	1
Left lung, lower lobe	2
Left lung, location not specified	1
Right lung, 6.	
Right lung, upper lobe	2
Right lung middle lobe	1
Right lung, lower l be	3

To summarize: Upper lobes, 4; middle lobes, 2; lower lobes, 5; location of cavity not specified, 1.

This small table shows the greater frequency of tuberculous cavities in the middle and lower lobes in infancy in our cases. If we consider the location of cavity formation in our own cases and of those collected from the literature, it will be seen that the lesion does not occur at the same location as it does in adults. In the majority of cases cavities in infants are deeply seated and usually at the root of the lung. In our cases cavities occurred more frequently in the lower and middle lobes than in the upper lobes.

IV. Report of Cases. Of the twelve autopsies performed on cases of tuberculous pulmonary cavities in infants at the Children's Hospital in the last sixteen and three-quarters years, 6 have come under our personal observation. It is these 6 cases we desire to report.

Case I.—Lillian R., aged six months, was admitted to the hospital on April 4, 1904. The family history was negative. The infant had been fed at different times on breast milk, condensed milk, and cow's milk. Although the patient had always been a delicate child, she had never had any serious illness. She was taken sick three weeks before admission to the hospital, with diarrhœa, weakness, and sweating at night. Four days before admission she developed a cough, coughing severely at times, and became extremely weak. The physical examination disclosed a bronchopneumonia in an emaciated, rachitic infant. The patient became weaker, the bowels continued loose, and the temperature irregular, until the child died, nine days after admission.

The *autopsy report*, abstracted, is as follows: Bronchocaseous pulmonary tuberculosis; tuberculous enteritis; tuberculosis of the liver and spleen. An emaciated colored infant with slight petechial eruption on abdomen. The left pleura shows a few tubercles on its parietal surface.

The left lung measures 11.5 x 6.5 x 3 cm., and weighs 70 grams. It is everywhere studded with grayish yellow tubercles, most of them small (millet seed), some few obtaining to larger size. Portions of the lower lobe are so thickly studded with tubercles as to sink

in water. The lung is mottled gray and dark red. The air-content is especially diminished in the lower lobe. There is hypostatic congestion in the lower lobe and the lower part of the upper lobe. The surface section is granular, moist, and glistening, of a mottled grayish color. Crepitation is diminished, while the consistence is firm and tenacious, with a bloodstained fluid exuding. The right lung weighs 108 grams. The air content is practically absent in the lower lobe, and a portion of all three lobes sinks in water. The lower lobe is consolidated, but is less thickly studded than the left lung with miliary tubercles. The lower part of the middle lobe also shows pneumonia. The upper part of the middle lobe and the upper lobe show much more thickly scattered tubercles. There is a cavity in the lower portion of the lower lobe posteriorly, containing caseous detritus. The bronchial lymph glands are everywhere enlarged. There is tuberculosis of the cervical, mediastinal, and retroperitoneal glands. Miliary tubercles in liver and spleen. Also a fatty liver and chronic follicular colitis.

CASE II.—John T., aged fifteen months, colored, was admitted to the hospital on April 5, 1904. The family history was entirely negative. Baby was fed since birth on skimmed milk. Until four days before admission to the hospital he was apparently well. During these four days he had profuse sweating cough, fever, and evident pain on touching the anterior chest wall. Examination showed a diffuse bronchopneumonia. Infant died three days after admission.

The *autopsy* findings, in brief, were as follows: Caseous bronchopneumonia; miliary tuberculosis of the lungs, pleura, omentum, liver, spleen, and the hepatic, mesenteric, bronchial, and retropharyneal glands.

Body of an emaciated, colored infant. The left lung measures 11.5 x 7.5 x 3.5 cm., and weighs 71 grams. The color is mottled gray; the air content is diminished in the lower lobe, but in the upper it is normal. In the upper part of the middle lobe there is a cavity 2.5 cm. in diameter, surrounded by tuberculous caseous infiltration. The walls of the cavity are irregular and bordered here and there with tuberculous caseous masses. The contents of the cavity are purulent. The pleura directly over the above area is adherent with recent fibrinous adhesions to the chest wall; on breaking these adhesions the cavity was ruptured. Scattered through the lower lobe, and less numerous in the upper lobe, are many yellow tubercles. The right pleura shows a few pearly tubercles on the parietal layer. The right lung measures 10.5 x 8. x 2.5 cm., and weighs 49 grams. This lung is not affected except for a number of yellow tubercles.

CASE III.—Moses C., aged six months, colored, was admitted to the hospital January 8, 1905. The father and mother are living and well; they have had two children, the patient and one other child which is dead. The cause of death given was teething(?). The

patient had been breast fed up to the time of admission. He has always been well until three months before coming to the hospital; during these three months the infant had a severe cough, but two days before admission cough became worse and great quantities of mucus were coughed up. The examination elicited the physical signs of a bronchopneumonia. The temperature was not hectic. In two days after admission the infant died.

The *autopsy* revealed: Caseous bronchopneumonia; general miliary tuberculosis; tuberculosis of the liver and spleen, and of the bronchial and mesenteric lymph glands.

The left lung weighs 145 grams. The entire lower lobe and the lower part of the upper lobe are consolidated. There is a large cavity 3 x 2 x 4 cm. in the upper third of the lower lobe posteriorly. It is superficial, and in one place a thickened pleura forms part of the wall. The bloodvessels and bronchi bridge across the cavity, and the walls are very irregular and dark in color. A small cavity, 0.5 x 0.5 x 0.5 cm., is also found on the lower surface of the lower lobe. There is an extensive obliterative diaphragmatic pleurisy at this location which brings the cavity close to the diaphragm. The whole lower lobe shows advanced caseous pneumonia, and also the greater part of the upper lobe, especially posteriorly. The air content is absent, except along the anterior border and at the apex. On both sides the bronchial glands are very much enlarged and caseous. Miliary tubercles in the liver, spleen, and intestines. The mesenteric glands are caseous.

Microscopic section of the lung close to the cavity wall shows diffuse cellular infiltration of tuberculopneumonic type. The type of cells present is lymphocytic, with a very few polymorphonuclear cells. There is congestion of the capillaries and giant-cell formation. The tissues in the immediate vicinity of the wall of the cavity show numerous large areas of typical caseation, but there is very little fibrous tissue formation. The large bronchial tubes in the neighborhood show marked bronchitis, the cellular exudate consisting of polymorphonuclear cells and lymphocytes. The walls of the bronchi show the infiltrating process.

CASE IV. Robert N., aged eleven months, colored, was admitted to the hospital November 28, 1905. The family history was negative; the mother and father living and well. There was only one other child, and it was well. There was no history of tuberculosis in the family. The baby's birth was normal, and up to the time of admission it had been fed exclusively on breast milk. It had always been well, with the exception of an attack of gastro-enteritis when six months old. For several months before coming to the hospital the infant had had a cough, which in the last two weeks had become much more severe. On admission the infant presented the physical signs of a bronchopneumonia. Two days later it became much worse, cough very severe, especially at night. It did not take its

feedings well and the bowels became loose. It began to vomit, and on one occasion the vomited material was streaked with blood. The infant died twenty-two days after admission.

The *autopsy* report was as follows: Caseous bronchopneumonia; general tuberculosis; tuberculosis of the liver, spleen, mesenteric and bronchial glands; tuberculous enteritis and peritonitis; chronic fibrinous pleurisy.

The left lung weighs 62 grams. It is slightly congested, and shows a slight amount of œdema. This lung contains a few scattered gray miliary tubercles. The bronchial glands are slightly enlarged. The right lung weighs 205 grams. The whole lung is consolidated, it is firm in consistency and grayish yellow in color. The surface section is smooth, dry, and dull. There is a cavity at the upper part of the middle lobe, external to the mid-clavicular line. The cavity measures 2 x 1 x 3.5 cm. in size and extends upward into the upper lobe. The walls of the cavity are dark in color and covered with granulations. In the upper lobe there is an excess of fibrous tissue. Over the right lung there is a chronic adhesive pleurisy. There is tuberculosis of the intestines, peritoneum, spleen, liver, appendix, and mesenteric glands.

A microscopic examination of the section from the wall of the cavity shows fibrous tissue and a cellular exudate consisting of polymorphonuclear cells and small lymphocytes. The tissue in close proximity to the cavity wall consists of an overgrowth of fibrous tissue which extends into the alveolar walls. Embedded in this fibrous tissue there are collections of typical tubercles; they are for the most part small and show a small amount of caseation. Giant cells are very prominent. The surrounding lung tissue shows the capillaries congested. Widespread caseation of the caseopneumonic type is not present. The process is a chronic fibrocaseous tuberculosis, with the presence of many giant cells.

Case V.—Lillian P., aged one year, colored, was admitted to the hospital May 27, 1907. The parents were living and well. There had been no other children. The patient's birth was normal, and until the time of her admission she had been breast fed. She had never had pertussis, measles, or any contagious disease. She had had fever for one month before coming to the hospital. Baby had been vomiting sour milk immediately after feeding several times a day. The bowels were constipated. For three days before admission she had a number of general convulsions lasting from five to ten minutes. Examination revealed harsh breathing all over the lungs, with many large moist rales. She had slight rigidity of the neck muscles and a positive Kernig's sign. By lumbar puncture 45 c.c. of slightly cloudy fluid was withdrawn, in which tubercle bacilli were found. Child died forty-eight hours following admission, after having had a number of convulsions.

The *necropsy* follows: Caseous bronchopneumonia; tuberculous

enteritis; tuberculosis of liver and spleen; tuberculous meningitis. The left lung is 10 x 8 x 3.5 cm., and weighs 80 grams. The pleura is normal. The surface section of the lung shows numerous small gray translucent tubercles, without bronchopneumonia. The tubercles are isolated. There is slight hypostatic congestion in the dependent parts. The lung is crepitant and exudes bloody fluid on pressure. Bronchi and pulmonary vesels are normal. The bronchial glands are greatly enlarged. The right pleura is congested and thickened. There are firm adhesions from the right upper lobe to the anterior axillary line, and from the middle lobe to the fourth rib. There are adhesions posteriorly over the upper lobe. The right lung measures 13 x 9.5 x 3 cm., and weighs 95 grams. Generally, this lung is the same as the left, with the exception of the upper lobe. The upper lobe contains a cavity 1.5 x 1.5 x 2 cm., situated 1 cm. from the apex, and another cavity below this at the base of the lobe measuring 2.5 x 2 x 1 cm. Surrounding these cavities the lung tissue in this lobe is consolidated by a caseous pneumonia. On pressure mucopus exudes. The liver shows fatty change, and there are translucent gray tubercles distributed throughout. The spleen contains a few gray tubercles. The small and large intestines show numerous tuberculous ulcers especially in the lower part of the ileum. The mesenteric glands are greatly enlarged, and some are caseous.

Case VI.—Braxton R., five moths old, colored, was admitted to the hospital February 6, 1907. His father, mother, and two sisters are living and well. Infant's birth was normal, and it had never been sick until six weeks before admission. During this time he had a severe cough. Mother states that a dark-colored discharge comes from the nose during coughing attacks. The physical examination revealed an emaciated colored infant, whose lungs showed numerous moist rales both anteriorly and posteriorly. A smear made from the throat, in order to obtain some expectoration, showed no tubercle bacilli. Heart and abdomen were negative. There was a small amount of blood in the bowel movements. Infant died eleven days after admission.

The *nercopsy* report follows: Caseous bronchopneumonic tuberculosis; general miliary tuberculosis; tuberculous pleurisy and peritonitis; tuberculosis of liver, spleen, kidneys, and intestines; fatty heart and kidneys.

The pleura on the left side is normal, but on the right side there are tuberculous adhesions. The left lung measures 9 x 5 x 3 cm., and weighs 45 grams. The air content is greatly decreased, and there are a number of large yellow tubercles scattered throughout the lung. The right lung measures 10 x 6 x 3.5 cm., and weighs 85 grams. This lung shows extensive pneumonia with many yellow tubercles, and tuberculous infiltration around the small bronchi. Crepitation is absent; the lung is firm in consistency, and the amount of blood is increased. At the right apex posteriorly the pulmonary

tissue is broken down, leaving a tuberculous cavity, 2 x 1 cm. On the parietal peritoneum are seen a number of discrete yellow tubercles, 3 mm. in diameter, having the appearance of bovine tuberculosis. There are miliary tubercles in the liver, spleen, kidneys, and intestines.

The six cases of cavity formation all occurred in negro infants between the age of five and fifteen months. Our experience bears out the well-known fact that the colored race is especially susceptible to tuberculosis, and the cases autopsied usually showed widespread lesions of an advanced type. Miliary tubercles were present in the lungs especially, and to a less extent in other organs. These lesions were usually small, in all likelihood an evidence of terminal infection, and were secondary to the larger lesions, either of the lungs or lymphatic nodes. The bronchial glands were tuberculous in all these cases. The pleura in our cases showed widespread adhesions or distinct miliary tubercles. No data were obtainable, either in the family or personal histories of the cases, which would indicate the source of the infection. In only one case had there been any disease prior to the fatal illness, namely, one infant having had an attack of gastro-enteritis (Case IV). Three of our cases had been fed exclusively on the breast until admitted to the hospital. The cavity formation in the lungs was with one exception of short duration, and occurred in the larger caseous areas of the lungs, and was not surrounded by fibrous tissue so commonly found in older children. In one case only was the process of longer duration, showing the formation of fibrous tissue around the borders of the cavity.

In conclusion we may say cavity formation does not occur with the same frequency in infants as in older children. In our own autopsies 16 per cent. of the infants dead from tuberculosis showed cavity formation: a far lower percentage than is reported by other observers. The type of lesion observed by us is not of the variety which lasts long enough to produce cavity formation. The infants usually succumb to the widespread process before the larger lesions have time to soften and their contents to be thrown off. In our cases tuberculous cavities in infants occurred most often at the root of the lungs, in the middle and lower lobes.

TWO CASES OF MYXŒDEMA.[1]

By Robert L. Pitfield, M.D.,
PHYSICIAN TO ST. TIMOTHY'S HOSPITAL, ROXBOROUGH, AND PATHOLOGIST TO THE GERMANTOWN HOSPITAL, PHILADELPHIA.

The nervous symptoms of myxœdema are so characteristic and often so profound as to lead one to consider whether the disease is not essentially one of the nervous system. In this respect the term myxœdema is not so good a designation for the disease as is hypothyroidea; and in general treatises if it is not classed among diseases of the thyroid it should have no place other than with nervous diseases. Even in complete cases, notwithstanding the fact that there are marked changes in the skin, the fundamental disability and real pathological conditions to be described and treated are in the central nervous system. It is probably some serious change in the nutrition of the nerve elements, and most of the symptoms are those of nervous exhaustion and malnutrition.

Case I.—With a diagnosis of neurasthenia, Mrs. F., a large, fattish woman, aged forty years, pale, careworn, lacrymose, and feeble, was admitted to the wards of St. Timothy's Hospital, Roxborough. Not only was she physically weak, but it was quite evident by a glance at her face that she was the subject of a profound neurosis. Her eyes were sunken, her eyebrows were arched upward, and her forehead was wrinkled. Indeed, the term "sorrowful fatigue," so aptly applied by Ewald, describes her expression so completely that it is not necessary to say more except that she was pale and her flesh flabby.

On pulling down the bedclothes, it was at once seen that the yoke of myxomatous tissue encircling her thorax was marked. Large pads of such tissue covered the abdomen, buttocks, and thighs. Her bones were small and her muscles ill developed and flabby. The skin of the legs and feet was somewhat dry and scaly.

She was of that type of middle-aged woman who had borne four children and had largely supported them by labor in a mill and as a washerwoman. It was quite apparent that the left breast was the seat of a slow-growing carcinoma. This fact, together with the subnormal condition of her blood and general nutrition, was responsible for her neurasthenic condition, which was indeed pitiable. She worried over trifles, cried at a look, nor could she sleep; her nights were restless and unrefreshing. Her memory was very poor and her carcinomatous breast was the source of much mental perturbation. Her knees creaked and crepitated when they were bent, and, what was highly significant, gave way under her from weakness to

[1] Read at a meeting of the Section on General Medicine of the College of Physicians of Philadelphia, March 6, 1909.

such an extent that she was prevented from walking very much. Of all the asthenic symptoms of this disease, this one may be singled out as perhaps the most marked and the one of which all patients complain the greatest. She had deafening tinnitus and visual hallucination, very common things for myxomatous patients to experience, as is the sensation of being cold constantly, even in summer; from the latter she suffered, inasmuch as her temperature was subnormal and her skin sensations deranged. She had no spade-like deformity of the hands, no supraclavicular pads, but her abdomen, breast, and thighs were covered with myxœdematous tissue that trembled when it was palpated; her skin was dry, bluish, lusterless, and scaly. She had a history of profuse uterine hemorrhages that were prolonged and exhausting. She has always been large, weighing at one time two hundred and ten pounds.

Her circulation was weak and her heart sounds clear but feeble, and while there were no adventitious sounds, and the size of the heart and its position about normal, the sounds had no tone. Her blood pressure was 110 mm. Hg. Her chest was emphysematous, her breath sounds weak. The liver and spleen were normal; the abdomen was pendulous and distended. She suffered from angenoid pains under the left breast. Her stomach was normal; there seemed to be some hypoacidity. She was always obstinately constipated and her tongue was thick and yellow. Her urine showed casts and albumin; there was no sugar. In 40 per cent. of these cases albumin and casts appear, only to disappear under thyroid treatment. Her blood examination was as follows: The red cells were 3,500,000, the white cells 12,400, the hemoglobin 44 per cent. A differential count of the leukocytes revealed: Polynuclears, 62.6 per cent.; small lymphocytes, 33.6 per cent.; large lymphocytes, 1.6 per cent.; and myelocytes and eosinophiles (each), 1 per cent. The blood platelets were increased. Normoblasts, poikilocytes, anisocytosis, and polychromatophilia also were noted. The presence of the carcinoma largely contributed to the anemia, and altered the blood picture.

Violent paresthetic pains in her calves prevented her from sitting or walking with any comfort. The major reflexes were normal, her pupils reacted normally, and her eye grounds were normal. There was no tremor. Her uvula was œdematous, as was her pharynx, and her voice was high pitched and strident.

Under two grains of thyroid extract and arsenic and iron for her anemia, opium for her insommia, aspirin for her pains, her condition improved wonderfully. She lost seventeen pounds, lost her depressing nervous symptoms and pains, she became stronger, slept well, was cheerful, and happy. Her voice became more soft and less strident, and with the disappearance of her myxœdema the sensation of cold gave way to normal sensations. Under the thyroid treatment she suffered from thyroidismus to the extent that

this drug had to be discontinued occasionally. This was characterized by fever, tremors, and palpitation of the heart, as it usually is.

Myxœdema is a disease of many symptoms, so much so that one may be confused and feel that he is merely dealing with a neurasthenic, rheumatic, fat woman, while in reality he is dealing with a disease that yields most readily to treatment. I have seen five cases of myxœdema, all of which were misdiagnosticated and accordingly mistreated for years. This is true also of the following case, that is typical of this disease in every particular:

Case II.—Mrs. G., aged sixty-two years, married, consulted me for an overpowering weakness of the knees, dyspnœa, rheumatic pains, most pronounced œdema of the face and trunk, and all but total deafness. Upon seeing her for the first time I was impressed by the fact that her face was not only œdematous, but was stolid, wooden, and what little expression illuminated her countenance was that of woful fatigue. The upper eyelids were so œdematous that they at times obscured her vision and hung over the palpebral fissure. They were so translucent as to suggest true dropsy, and many physicians had been led to believe that she was far advanced in renal disease. In order to attempt to see she was compelled to wrinkle her forehead so that her brows were arched continually. Her face was squarish and there were reddish patches over each cheek bone.

She told me that her weight was two hundred and two pounds and she was five feet two inches in height. Not only was she so deaf that I was compelled to shout in her ear, but her mentality was dull and slow; and she suffered extremely from the cold. She is the mother of nine children, and her illness began shortly after the last child was born, near the menopause. She had previously been a robust, healthy woman of good family and personal history.

A careful physical examination showed, in addition to the myxœdematous face, deafness, and dull mind, solid œdema of the trunk and extremities. Her skin was dry and scaly; especially over the extensor surfaces it was thickened, dry, and coarse. When she removed her stockings the floor was often strewn with scales. She suffered from roughness of the skin and dandruff. In places the skin was waxy, translucent, and jelly-like. Above the clavicles and in the anterior axillary folds there were marked pads of myxœdematous tissue. Vast masses of this tissue formed a yoke over her thorax, her abdomen was distended and pendulous and covered with a myxœdematous pad. The axillary and pubic hairs were all but gone, and her eyebrows were scanty and thin. The outer half was characteristically (as Hertoghe has shown) thinner than the inner half. Palpation of the thyroid showed a very small organ; indeed, it is very doubtful if it was felt at any time. There was true œdema (dropsical) of the legs, due to her weak heart. Her joints were the seat of violent pains at times, and creaked and crepitated when they

were flexed and extended. Her voice was raucous and harsh and her speech slow and scanning. Her uvula and pharynx were œdematous and translucent.

Examination of her heart showed that its impulses were weak and feeble, though rythmic; while it was difficult to define the area of dulness, it was quite apparent that she suffered from a dilated heart and a degenerative myocarditis. There were no adventitious sounds; the systolic sound was feeble and the second decidedly unaccentuated, showing a very weak vascular tone, as the blood pressure (90 mm.) showed. Her lungs were slightly emphysematous, but there were no other evidences of any changes in the structure. The liver and spleen were normal in size. Her digestion has always been poor, and she evidently has suffered from hypoacidity. She has suffered from most obstinate constipation at all times.

Her nervous symptoms were striking and gave her the most trouble. She had a dull brain as well as dull hearing; indeed, her memory was so poor and perceptions so slow that her daughter told me that she had to serve as brains and ears for her mother, and it quite wore her out to have to talk to her. Not only was her hearing bad, but she suffered from tinnitus to such an extent that she often summoned her family to answer the telephone when in reality no bell rang; she often heard pistol shots in her ears; she had hallucinations of sight, and frequently thought she saw people in her room when none were present.

Her temperature was 97° when first seen, and in the summer she hugged the fire and wore extra wraps in order to keep warm. This is as characteristic of myxœdematous cases as pyrexia is of typhoid fever. She perspires at times unevenly; the perspiration will stream from one area of the skin and nowhere else, dropping at times from her forehead to the floor.

The major reflexes were normal, there was no Babinski's or Kernig's sign. Her pupils were small, equal, and sluggish to light; her station is fair, her gait unsteady; her sensations were diminished, and motor apparatus weak. All fine movements were clumsy and awkward. She fell at the slightest provocation, and her knees gave way under her. She had constant backache and joint pains. Under her left breast she had characteristic anginoid pains. Her gait was awkward and hippopotamus-like. Her urine was absolutely normal in every particular, it had a specific gravity of 1020, was acid, and devoid of sugar, albumin, and casts.

Her blood was in surprisingly good condition considering the length of her illness: Hemoglobin, 88 per cent.; red cells, 3,560,000; white cells, 7600; the color index 1.1. A few normoblasts were found. I have found these in all four cases of myxœdema.

She had no history of anything amiss with the pelvic organs, except about the menopause there was a period of severe uterine hemorrhages which lasted for weeks.

Her eyes were carefully examined by Dr. Wendell Reber, who found nothing abnormal for a woman of her years. Dr. Reber also found that the poor hearing was due to poor air conduction and probably to some labyrinthine involvement. Myxomatous infiltration of the pharynx and Eustachian tubes was probably the cause. Her nose and throat were highly myxœdematous. She was troubled for some time by attacks of constant sneezing.

It was as if a large heavy blanket had been cast all over this woman, weighing her down and interfering with all movements and with her senses of sight and hearing, and instead of keeping her warm it made her cold and caused her to be dyspnœic and oppressed.

Under 2 grains of thyroid extract three times a day this woman improved wonderfully; at the end of a month she was well except for her weak heart. Her hearing was restored to the extent that she could take part in all conversations in her rooms in ordinary tones. Her voice lost its raucous tones and the scanning speech disappeared. The pains in her back and joints were dispelled, her countenance lost its stolidity and œdematous appearances, and she became bright and animated. Her weight was reduced to one hundred and seventy-eight pounds in a month. The thyroid had the effect of causing her to feel warm and nervous. Once or twice she suffered from thyroidismus with fever tremor and rapid pulse. After six weeks' treatment with thyroid, digitalis, and massage her myxœdema disappeared completely, and save for a weak heart and pulse of 92 and slight tinnitus in damp weather, she has no symptoms. The thyroid caused her hair to fall out and her hands to scale excessively, but her hair began to grow immediately.

After thyroid extract nothing does these patients so much good as massage; it was the only thing that seemed to help this woman before she took the thyroid extract.

FATAL ANEMIA OF UNKNOWN CAUSE IN A CHILD OF FIVE YEARS, WITH UNUSUAL CELLS IN THE BLOOD.

By Williston W. Barker, M.D.,
of Dorchester, Massachusetts.

On December 8, 1908, I was asked to examine the blood of a patient with the following history:

C. B., a female, aged five years, white, adopted, but of known and healthy parentage, had always been a particularly healthy child, except for a capricious appetite. Three months ago she had a mild attack of measles without evident sequels. For four or five weeks she had been pale and listless. Ten days ago three small

purplish spots appeared on her face, fading gradually. Four days ago a blood stain was found on her pillow, and its source was determined to be an oozing gum which she had picked. Next day, by advice of the family physician, a dentist packed the gum, without result; on the following day, a gutta-percha packing did control the bleeding over night, but on December 8 it began again. On December 7 fresh purpura was observed on the legs. The whole amount of blood lost was very slight, there never being any active hemorrhage or clots seen.

Physical examination showed a well developed and nourished child, with moderate, slightly yellowish pallor of the skin. The mucous membranes were of fair color. No glands were felt. The teeth were good; the throat was normal. Thin blood was adherent to the left upper gums, which were not swollen or necrotic. A loud systolic murmur was heard all over the cardiac area and in the neck; the heart was not enlarged. The pulse was of notably low tension. The lungs, liver, and spleen were normal to physical examination. There were three small greenish purpuric spots on the face, two on the back, one on the front of the chest; many large purple spots were found on the legs and thighs. The temperature was 99°, the pulse 80, the respirations 20. The urine was pale, alkaline, had a specific gravity of 1006, and albumin, sugar, blood, diacetic acid, and acetone were absent. The stool was free from blood by the benzedin test.

The child failed progressively, and died January 27, 1909.

Treatment, consisting of out-door life, forced feeding, orange juice, electricity, and various drugs, was entirely ineffectual. The temperature was constantly elevated, reaching 103.5° at night. From January 5 to January 15 there was an attack of chicken-pox, with vomiting and rapid loss of strength. There was temporary diplopia about December 15. There were a few more purpuric spots at intervals, and once there was slight epistaxis. During the last two weeks of life there was slight œdema of the face and ankles and an extraordinary swelling of the gums, which almost completely covered the teeth. No glands were ever felt, except a few under the jaw after the swelling of the gums. The spleen was never demonstrably enlarged. The urine contained a trace of albumin at one examination. Death in coma followed twenty-four hours of active delirium. An autopsy was not permitted.

The blood (see table) showed a marked and progressive poverty of all the myelogenic elements (red cells, polynuclear leukocytes, and platelets). Toward the last there were many very young basophilic cells, and many erythroblasts. There was marked macrocytosis from the first, but comparatively little variation in the shape of the red cells. Polychromatophilia was extreme, but stippling was absent. No eosinophiles or mast-cells were ever seen. The coagulation time on December 8 was the same as my own—three and one-

Fig. 1

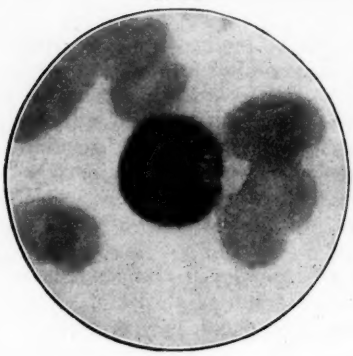


Fig. 2

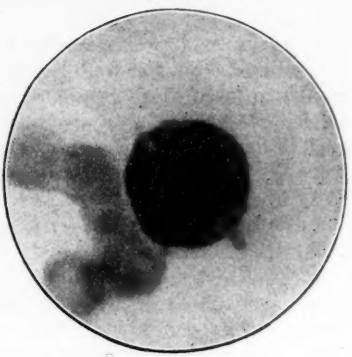


Fig. 3

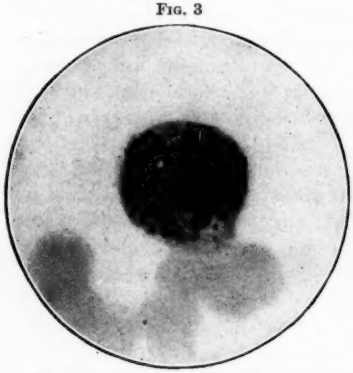
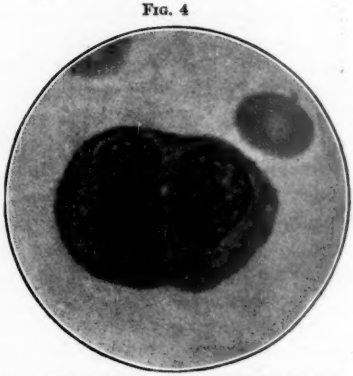


Fig. 4



Figs. 1 to 4 are cells from the blood. In No. 1 two rods are shown plainly, forming an *X*, and several above that are less distinct. In No. 2 the rods form a *Y*, while in No. 3 they are scattered all over the cell. In No. 4 the rods are less clear, but there is a large double nucleus.

Fig. 5

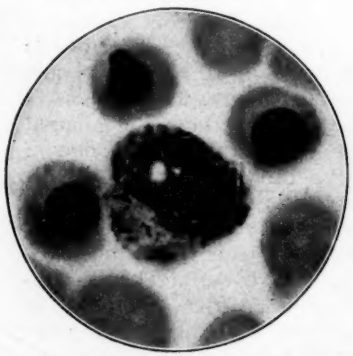
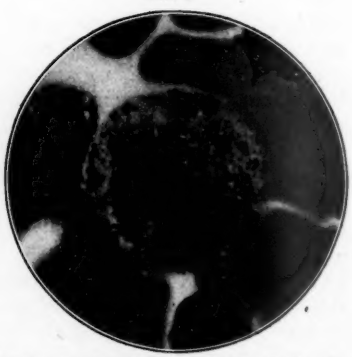


Fig. 6



Figs. 5 and 6 are cells from crushed fœtal liver tissue, prepared and stained like the blood smears. They both show scattered rods, and No. 6 shows a nucleus in division. × 1500 diameters. (Wright's stain.) (Photomicrographs by L. F. Brown, of the Massachusetts General Hospital.)

half minutes. A marked serum ring appeared on the Tallqvist paper, on January 5.

BLOOD EXAMINATIONS, C. B.—1908–1909.

	Hemoglobin per cent.	Red cells	White cells	Platelets	Polynuclear neutrophiles per cent.	Lymphocytes per cent.	Young basophiles, per cent.	Myelocytes, per cent.	Special cells, per cent.	Erythroblasts per 100 whites	
										Megaloblasts	Normoblasts
Dec. 8, 1908	65	3,360,000	2100	Very few	15.0	82.0	0.0	3.0	0.0	0.0	2.0
" 15, "	60	2,216,000	1900	Very few	5.0	93.0	0.0	2.0	0.0	3.0	0.0
" 22, "	60	2,212,000	1300	Absent	2.5	95.5	0.0	2.0	0.0	1.0	0.0
" 29, "	65	1,776,000	1500	Absent	6.0	90.0	1.0	3.0	0.0*	8.0	3.0
Jan. 5, 1909	45	1,568,000	3100	Absent	1.0	90.0	9.0	0.0	0.0*	0.0	0.0
" 20, "	20	944,000	4300	Absent	2.5	42.5	53.0	0.0	2.0	7.0	6.0

* In count of 200 whites.

In the smears taken January 20, and rarely in those of January 5 and December 29, there were found certain cells of which I have not been able to find a published description. Dr. J. H. Wright, who was kind enough to examine the smears, had observed similar cells in the liver of a four months' fœtus about two years ago. These cells (Figs. 1 to 6) are large, rounded or oval, with from one to three vesicular neutrophilic nuclei and pale basophilic protoplasm; in the protoplasm there is more or less coarse granular material staining a deep red; in some of the cells this material takes the shape of straight or slightly curved rods, some of them beaded. That these rods are not artifacts is proved by their appearance in many smears, stained with different bottles of stain and by different persons. They are similar to rods seen in the protoplasm of lymphocytes in a case of acute lymphatic leukemia reported by Auer,[1] but the cells are not lymphocytes, nor prelymphocytes. In the absence of postmortem evidence I venture no hypothesis as to the place of these cells in blood formation. They are obviously young cells, many of them in active division, but none of them show evidence of phagocytic activity. It is equally futile to discuss the classification of the case. There was certainly grave impairment of the cell-producing activity of the bone-marrow, but not of the aplastic type. Leukemic metaplasia of the bone-marrow is not an impossible explanation.

The case is reported partly because of the rarity of fatal anemia in early childhood similar to the "pernicious" anemia of adult life, and partly to place on record the appearance of the cells described. I wish to acknowledge my indebtedness to Dr. J. T. Sherman, of Dorchester, for allowing me to make this report; to Dr. J. H. Wright and Dr. R. C. Cabot for helpful advice and information; and to Mr. Brown for the illustrations.

[1] AMER. JOUR. MED. SCI., 1906, cxxxi, 1002.

THE OCULAR COMPLICATIONS OF NASAL SINUS DISEASE.[1]

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The most striking and probably the best known orbital complication of nasal sinus disease is that due to a dilatation of the frontal and ethmoidal sinuses without inflammatory signs, the so-called mucocele, which causes a mechanical displacement of the orbital contents. The eyeball is generally uninvolved. The distention which the sinus undergoes is associated with rarefaction of the bone, usually of the inferior wall. On the other hand, in a case which I recently operated upon, the upper or cerebral wall of the frontal sinus was absent and the altered mucous membrane of the dilated sinus was directly adjacent to the dura of the anterior cranial fossa. The only treatment is operation, and is usually simple, as the long-standing displacement of the eyeball permits very free access to the nasal structures. The operation[2] consists in the removal of the lower wall of the frontal sinus and of the entire ethmoid labyrinth, thus permitting free drainage into the nose.

Inflammation of the sinuses is associated with external or orbital inflammatory signs whenever the inflammation invaded the intervening bony wall. In the mild cases there is no macroscopic change in the bone, but a periostitis is present over the floor of the frontal sinus with swelling and redness of the eyelid or over the ethmoidal os planum, causing exophthalmos. This condition may resolve of itself or on intranasal treatment. If the involvement of the bone is more active a discoloration or a circumscribed defect in the bone will occur usually in a typical site in the floor of the frontal sinus or at the ethmoidal os planum. The pus thus gains its way to the periosteum and forms a subperiosteal orbital abscess which either remains encapsulated or may extend forward and perforate the skin of the eyelid; the suppuration may then cease, the wound heal, or a purulent fistula remain. The orbital contents are generally not involved in these cases beyond slight venous congestion at the optic disk, as the periosteum is easily detached from the bone and protecting granulations spring up.

Subperiosteal orbital abscesses are not infrequent in children, the infection being transmitted by the ethmoid labyrinth. In operating upon these cases a curved incision is made along the inner orbital margin; on retracting the periosteum the small collection of

[1] Read at a meeting of the New York Academy of Medicine, December 3, 1908.

[2] Arnold Knapp, The Surgical Treatment of Orbital Complications in Diseases of the Nasal Accessory Sinuses, Jour. Amer. Med. Assoc., July 25, 1908.

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pus will be encountered between the periosteum and the bone and usually a small irregular defect in the os planum. The opening in the bone should be slightly enlarged and the contiguous ethmoidal cells curetted; the case then heals without deformity.

If the orbital periosteum itself is invaded, which is most likely in the places where it is normally adherent, as for the passage of vessels, involvement of the orbital structures results, cellulitis or abscess. The optic nerve becomes inflamed and the ophthalmoscopic changes at the nerve head may be more pronounced on the nasal side. This was especially noticed in one of my cases in which the lesion in the orbital periosteum corresponded exactly to an area of necrosis just below the posterior ethmoidal foramen. The orbital condition recovered after the ethmoidal focus was removed.

The important and preponderating part played by nasal sinusitis in producing orbital cellulitis and abscess has, strange to say, only been recognized within the last years. Birch-Hirschfeld,[3] in an elaborate statistical research, concludes that nearly all orbital inflammations are caused by nasal sinus empyema. Under these circumstances the usually practised blind incisions into the orbital cavity are not surgical; the treatment should be based on the lines of the orbital operation for nasal sinus empyema, aiming at broad exposure by an incision along the orbital margin, careful inspection of the orbital walls, and proper drainage according to the individual case.

The importance of the maxillary antrum in causing orbital complications has in my mind been exaggerated. Disease of the antrum itself rarely seems to cause an orbital complication unless through the intermediation of the ethmoidal cells. The extension much more frequently follows a periostitis of one of the walls, as after an alveolar abscess. Thrombophlebitis of the orbital vessels, according to Uhthoff, is unusual after accessory sinus disease, and is more frequent from extension of a process in the face.

A very important group of ocular complications of nasal sinus disease are those of the optic nerve. That the optic nerve sometimes suffers in sphenoidal sinusitis has been known for some time, and brilliant cases of restoration of sight have been recorded by Holmes and others by timely treatment of the sphenoidal sinus. The recent investigations of Onodi[4] have shown that the optic nerve frequently is in close relation to the posterior ethmoidal cells and that the extreme thinness of the intervening wall makes the involvement more likely than in the case of the sphenoid. Cases have been observed that bear out the frequency of this involvement. Of especial interest is that the optic nerve is involved in the form known as retrobulbar neuritis in which a central scotoma is the characteristic functional defect. It is not known why this particular bundle of optic nerve

[3] Versamml. Deut. Naturf. und Aerste, Dresden, 1907.
[4] Der Sehnerv und die Nebenhöhlen der Nase, Vienna, 1907.

fibers is first and principally involved. The optic nerve shows in the beginning no ophthalmoscopic changes unless the nasal infection is situated in the anterior ethmoidal cells, as in a recent case of well-marked papillitis with central scotoma, which I had the opportunity of following together with Dr. Coakley. The prognosis in these cases is excellent, and now that ophthalmological attention has been focussed on this interdependence of the nose and the eye, some of the hitherto obscure cases of acute retrobulbar neuritis will be recognized and nasal treatment promptly instituted.

Ocular paralyses are not infrequently the only manifestations of orbital complications. In a case of grippe with ethmoidal involvement which came under my observation the internal rectus for a time was paretic.

Neuralgia, especially ciliary and retrobulbar, is frequently due to sinus affections, and asthenopia is a common symptom. According to Kuhnt,[5] muscular asthenopia, accommodative asthenopia, and contraction of the visual field, are the functional disturbances observed in nasal empyema in the order of their frequency; he believes them to be due to absorption of toxins from the purulent focus in the sinus.

There is a group of eye affections comprising iridochoroiditis, glaucoma, and detachment of the retina, with which certain authors have brought sinus disease in etiological relation. Some over-enthusiastic observers have even cured these conditions by surprisingly insignificant operations on the nasal sinuses. This is a subject upon which we require additional information. Kuhnt, whose experience is surely great, states in the above-quoted article that he has never seen a case of iritis or choroiditis caused by sinus disease, but thinks that cyclitis, especially the form chiefly characterized by opacities of the vitreous, can depend on this cause. He has never observed glaucoma to be caused by nasal disease, but believes that in predisposed eyes an attack may be brought on by a sinus affection. A number of cases of this kind have been observed. The reported cases of detachment of the retina associated with nasal sinus disease are not convincing.

That the list of ocular disturbances which can be produced by sinus affections is not exhausted there can be no doubt, and a great deal of careful work needs still to be done to complete our knowledge of the relation of nasal sinus disease to disease of the eye.

[5] Deut. med. Woch., 1908, No 37.

THE CAMMIDGE REACTION IN EXPERIMENTAL LESIONS OF THE PANCREAS.[1]

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Although abundant clinical proof has been afforded his reaction by Cammidge, it has thus far remained for others to publish results of work conducted along the fundamental lines of chemistry and experimentation. Reports of experimental studies have by no means kept pace with those derived from clinical observation, which is the more to be regretted since the value which would accrue from the establishment of a diagnostic measure in pancreatic disease is inestimable and demands a firm experimental basis before it can be accepted.

In a preliminary report[2] we published results of some studies of the Cammidge reaction in experimental pancreatitis, using the "C" reaction, which had given good clinical results in the hands of one of us.[3] Up to that time no report of experimental work had appeared in which this modified reaction had been used, but since our first report Eichler and Schirokauer[4] have published results of some experimentation in dogs, using the "C" method. Their work has left them somewhat in doubt as to the usefulness of the test, the crystals appearing at irregular intervals even when definite pancreatic lesions existed.

The work which we report at this time was undertaken to confirm or to refute Cammidge's claims, that by means of chemical analysis a specific substance could be demonstrated in the urine of individuals suffering with pancreatic disease. This specific substance was thought by Cammidge to be glycerin, absorbed into the circulation during the process of fat necrosis and excreted finally in the urine. This hypothesis was soon abandoned for the present belief that the substance which is isolated by means of phenylhydrazin is a pentose, not found as such in the urine, but obtained from some mother substance by hydrolysis with hydrochloric acid. What this mother substance may be is not stated, but its origin is thought

[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 11 and 12, 1909.

[2] Amer. Jour. Med. Sci., January, 1909.

[3] Annals of Surgery, February, 1909.

[4] Berl. klin. Woch., 1909, p. 352.

to be from the pancreas, which, as is well known, contains a relatively large amount (2.48 per cent.) of pentose-yielding material.

We have endeavored in our series of cases to imitate the acute and chronic types of pancreatitis met with in human beings. The first is easily done by the injection of oil into the pancreatic duct, while the morbid changes seen in the second type of pancreatic lesion were closely simulated by simple ligation of the duct of Wirsung. All of our experimental animals were dogs, and before operation they were confined for from one to more days in a cage used for metabolic studies. The food consisted of meat, potatoes, bread, and water. The urine was collected for twenty-four hours preceding operation, and in every instance, with the exception of three of our early animals, it was examined for albumin, sugar, and the Cammidge reaction. Albumin was tested for by the Heller's test, and if present was removed by heat and acid. Sugar was tested for by Fehling's and Nylander's methods, and the Cammidge reaction was performed according to the directions given in Robson and Cammidge's book.[5] This is the so-called "C" reaction. It may be stated parenthetically that albumin was almost a constant constituent of the dogs' urines; sugar was never found before, and with the exception of our extirpation series, never after operation; and the Cammidge reaction was found but once before operation, this dog, of course, being discarded as valueless in our experiments.

Operation was performed under aseptic conditions, ether being used as an anesthetic. Postoperative suppuration was never seen, although no dressing or protection was given the wound. The urine obtained after operation was examined for albumin, sugar, and for the Cammidge reaction. Seventeen dogs were studied—six for acute pancreatitis, four for the effects following ligation, two for the effects following extirpation of half of the pancreas (tail), three for the effects following crushing of the tail of the pancreas, and in two dogs a total extirpation was performed.

SERIES I.—The pancreatic lesions in this series were induced by the injection of from 10 to 30 c.c. of cotton-seed oil into the pancreatic duct, a procedure which causes rapid necrosis of the pancreas.

Dog 1. The urine before operation was not examined. The dog was killed eight hours after operation, and the urine collected up to that time gave a positive reaction. Macroscopic examination of the pancreas showed a diffuse necrotic process which involved most of the organ. A microscopic study revealed complete destruction of the tissue.

Dog 2. The urine before operation showed no Cammidge reaction. The dog was killed eight hours after operation, and the urine failed to show a positive reaction. The pathological examination of the pancreas showed neither macroscopic nor microscopic

[5] The Pancreas, its Surgery and Pathology. 1907.

lesions, as the attempt to inject oil into the pancreatic duct had been unsuccessful.

Dog 3. The urine before operation was not examined. The dog was killed eight hours after operation, and the urine collected up to that time showed a positive reaction. The postmortem examination of the pancreas revealed a diffuse necrotic process; lesions similar in nature were seen microscopically.

Dog 4. The urine before operation showed no Cammidge crystals. The urine after operation gave a positive reaction. The dog was killed eight hours after operation, and the macroscopic and microscopic examination of the pancreas showed a diffuse necrotic process.

Dog 5. The urine before operation was not examined. The urine after operation gave a positive reaction. The animal was killed eight hours after operation, and the pancreas was found to be necrotic except at the tail. Microscopic examination of the head revealed complete necrosis of the tissue, with hemorrhagic and leukocytic infiltration. In the tail there was marked parenchymatous degeneration and a few areas of necrosis.

Dog 6. The urine before operation showed no Cammidge reaction. The urine the first hour after operation was negative; four hours after operation it was positive. The dog was killed at this time, and the usual necrotic appearance following oil injections was seen. On microscopic examination, normal tissue was nowhere visible except in the tail.

SERIES II.—The pancreatic lesions in this series were caused by ligation of the pancreatic duct.

Dog 7. The urine before operation was negative for the Cammidge reaction; the urine the first day after operation was negative; the urine the second day after operation gave a positive reaction; on the third, fourth, and fifth days, positive reactions were obtained. The dog was killed seven days after operation, and an area of induration was found in the head of the pancreas opposite the point of ligation. The lesion, which was the size of a large walnut, was distinctly hard, and cut with greater resistance than the remaining portions of the gland. Microscopic study of the indurated tissue showed a subacute inflammatory process, which had caused small areas of necrosis in the acini. A leukocytic infiltration, consisting for the most part of round cells, was seen in the stroma and, to a less extent, about the acini. Proliferated connective tissue cells were also noted.

Dog 8. The urine before operation showed no Cammidge reaction. Positive reactions were obtained on the first and second days following operation. The dog was killed on the second day, and the pancreas was found to be indurated in an area about the size and shape of a hickory nut, the lesion being directly above the ligature, which still surrounded the duct. Microscopic examination

revealed changes similar to those seen in the preceding case, but not so extensive.

Dog 9. The urine before operation was negative for the Cammidge reaction. Negative reactions were obtained on the second, third, and fourth days following operation. On the fifth and sixth days after operation an attempt was made to open the pancreatic duct at the point of ligation, but was unsuccessful, owing to the induration about the duct. The first day after the second operation the urine was lost; on the second and third days the reaction was negative. On the fourth day typical crystals were found, and on that day the dog died. The urine collected on this day up to the time of death gave a negative reaction. Owing to advanced decomposition the pancreas was not examined microscopically. We are unable to explain the irregularity in the appearance of the crystals in this case.

Dog 10. The urine before operation was not examined. The first day after operation it was negative, but positive reactions were obtained on the second and third days. On the third day the duct was again exposed, the ligature cut, and the intestine opened. A probe was inserted in the duct and a point of resistance was encountered 1 cm. from the ampulla. Gentle pressure overcame the resistance and the probe was advanced still farther. On withdrawing it the same resistance was again met with. The head of the pancreas felt decidedly indurated. The urine following this second operation was so scanty that it could not be examined. On the second and third days negative reactions were obtained; on the fourth day a positive reaction, on the fifth a negative, on the sixth and seventh days positive reactions, and thereafter negative reactions were obtained. On the fifteenth day after the first operation, or twelve days after the second operation, the abdomen was again opened, and the omentum was found to be so adherent that it was impossible to locate the pancreatic duct. The dog was killed five days later, or on the twentieth day after the first operation; the pancreas was very much indurated and the duct could not be found. A microscopic examination was not made.

Series III.—In this series the tail of the pancreas was extirpated to a point immediately below the pancreatic duct.

Dog 11. The urine before operation gave no Cammidge reaction. The day following operation no reaction was obtained, but on the second day typical crystals were seen. The animal died three days after operation, and the autopsy disclosed a necrotic condition of the pancreas. The duct was found to have been ligated, so that this case can not be properly regarded as an example of the results following partial extirpation, but rather as an instance of incomplete extirpation plus ligation. Microscopic sections from the head of the pancreas showed well-preserved cells, the nuclei being slightly obscured by cloudy swelling. Small areas of liquefaction necrosis

were seen, and considerable hemorrhage was present in the tissues.

Dog 12. Urine before operation was negative. No pancreatic reaction was obtained on the first, second, third, fourth, fifth, and sixth days. Thereafter, until the nineteenth day, positive reactions were found. On that day the dog was allowed to run out of doors, and through carelessness the animal escaped. Examination of the excised portion of pancreas revealed a normal gland.

SERIES IV.—In all the cases in this series the tail of the pancreas was crushed with a hemostat in six places.

Dog 13. The urine before operation was negative. On the first, second, third, fourth, and fifth days positive pancreatic reactions were obtained. The dog was killed six days after the operation. The pancreas showed induration of the head and some injection about the tail, but no fat necrosis was apparent. Microscopic examination of the head of the pancreas showed some increase of connective tissue around the acini. The parenchyma seemed normal in appearance.

Dog 14. The urine before operation was negative. No urine was obtained the first day after operation. On the second day the urine was negative, but on the third and fourth days positive reactions were obtained. The dog was killed on the fifth day after operation. The tail of the pancreas was hemorrhagic and necrotic. The head was slightly indurated, the duct patulous. On microscopic examination the tail showed advanced necrosis of the cells, the head being practically normal.

Dog 15. The urine before operation was negative. Up to the sixth day after operation no Cammidge reaction was obtained; on the sixth and seventh days positive crystals were seen. The urine was not studied again until nineteen days after operation, when it was negative for the pancreatic reaction. Two days later, when we intended to kill the animal for the purpose of macroscopic and microscopic examination of the pancreas, we found that the dog had been removed from the cage and had been disposed of, so a pathological report on this case cannot be made.

SERIES V.—In this series a total extirpation was attempted.

Dog 16. The urine before operation was negative. The animal died the day following operation, and the urine collected up to that time gave a positive pancreatic reaction. Examination of the pancreas revealed a normal condition of that gland.

Dog 17. The urine before operation was negative. On the first and second days after operation positive reactions were obtained. The animal died on the second day. The pancreas seemed normal on microscopic examination.

We were led to believe from the results obtained in Series I, and from those seen in Dogs 7 and 8 (Series II), that occlusion of the pancreatic duct was the principal causative factor in the production

of the Cammidge reaction. We tried to establish this fact by removing the obstruction in the remaining two dogs of the second series, but were unsuccessful in Dog 9, and in Dog 10 positive reactions were obtained after two negative days. This may have been caused by a closure of the duct, but we have no means of verification, as there were so many adhesions that the pancreatic duct could not be located.

The view that occlusion of the duct might be the main cause of the appearance of Cammidge crystals had to be abandoned after we had completed Series III and IV, as the duct was left patulous in these cases, except in Dog 11 (Series III), and positive reactions were obtained in each case.

Cammidge has asserted that pentose is the specific substance which he isolates from the urine by his method, and that the pentose has its origin in the pancreas. We are not in favor of this view, for, were this correct, we should not expect to find typical crystals after total extirpation of the gland. We are inclined to believe that the substance found by the use of Cammidge's technique is but an expression of disturbed carbohydrate metabolism, this disturbance being referable to morbid changes in the pancreas. We have made no investigations along the lines of chemistry, but the melting point of the crystals found in one case was between 150° and 155° C., which is about the melting point of the phenylhydrazin compound of glycuronic acid.

Conclusions. 1. The Cammidge reaction is a constant feature in hemorrhagic pancreatitis, in mechanical injuries of the gland (crushing of the tail, partial extirpation), and in total extirpation.

2. In certain cases of the subacute type of pancreatitis the reaction is inconstant.

3. The nature of the phenylhydrazin compound is not definitely established. If pentose, it is apparently not derived from the pentose-yielding material of the pancreas.

4. A positive reaction is indicative of altered carbohydrate metabolism due to disturbance of the internal secretion of the pancreas.

THE TONSILS AS ELIMINATIVE ORGANS.

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The true functions of the tonsils and other adenoid structures abutting on the mucous membranes is a problem nearly as obscure today as it was twenty years ago. They were then supposed to secrete a substance which facilitated swallowing the bolus of mas-

ticated food, and also to prevent in some obscure way the entrance of infectious materials into the body.

Francis R. Packard[1] writes: "The faucial tonsils are really a large pair of lymphatic glands, the functions of which are but imperfectly understood. As with other lymph glands they probably protect the organism from infections of various kinds by acting as filters, and by in some way lessening the toxicity of microörganisms which come within their sphere of activity."

This seems to represent the sum and substance of the ancient and modern teaching in regard to the matter. But it is somewhat incomprehensible why the microörganisms should enter the tonsils at all, when it is to be supposed that they might just as easily slip by unharmed, into the pharynx and œsophagus. If there were such a thing as ciliated epithelium in the follicles and crypts of the tonsils, one might imagine a continuous current such as exists in the Fallopian tubes, sucking them in against their will. And yet the crpyts of the tonsils even in health are found loaded with a varied flora of pathogenic and non-pathogenic germs—Loeffler's bacilli, pneumococci, streptococci, and staphylococci in pleasing variety. The natural supposition would be, since the nose is constantly exposed to atmospheric infections, and the mouth to those brought by the food and otherwise, that many of these microörganisms failing to penetrate the mucosa of the nose and mouth find lodgement in the tonsillar crypts. This, however, is a very unsatisfactory explanation of their presence there.

The tonsils are composed as we know of adenoid tissues, resembling that of the internal lymphatic glands, as distinguished from the superficial, or those abutting on the mucous membranes, such as the lingual follicles, the tonsils, the solitary and agminated glands of the intestine. The great and evident difference is this, that the superficial lymphatic glands have no direct connection with the lymph vessels, while the deep lymphatic glands are directly in the course of these, and are penetrated by them in all directions. The superficial lymphatic glands are, however, surrounded at their bases by wide lymph spaces, and are described in works of anatomy and physiology as "hanging into" these lymph spaces which communicate by small channels with the larger vessels. That the superficial lymph glands are different in their functions from the deep glands may be inferred from their different arrangement in this respect and from the fact that the deep glands are often found enlarged without any corresponding enlargement of the superficial glands, which may be supposed to be connected indirectly with the same system of channels. The superficial lymph glands have a free blood supply, thus being connected intimately with the blood circulation.

Physiologically there is a certain similarity between the superficial

[1] Osler's Modern Medicine, 1907, iii, 596.

and the deep lymph glands, in that they both have "germinating centres" whence issue enormous numbers of wandering leukocytes. In the deep glands all these leukocytes are poured into the lymph channels whence they are carried into the venous circulation. With the superficial glands the course is different. Some of them are poured into the surrounding lymph spaces, whence they may eventually reach the lymph channels and the venous circulation; but a vast number of them penetrate between the epithelial cells covering the glands, thereby causing an outward current. It is with these escaping leukocytes and the part they play that we are now concerned. Their outpouring into the crypts, and their being found there together with innumerable microörganisms is probably more than a coincidence. It might be regarded as a never-ending succession of sorties by the defenders of the body against the invading horde of microörganisms, and the crypts and surfaces of the glands might be regarded as the battle ground where the infection or protection of the body is decided. But why should the invading microörganisms select such a well-defended part for their onslaught? There lies the whole improbability of the idea.

W. G. McCallum[2] says of the mode of invasion in primary intestinal tuberculosis, "the bacilli adhere to the mucosa, and work their way into its substance. Orth holds that the lesion begins always in the lymph nodules. . . . The first change is of the appearance of tubercle nodules in the substance of the mucosa and very frequently in the lymphoid nodules, or Peyer's patches."

Now so far as we have any positive knowledge, there is no proof that the superficial lymphatic glands ordinarily absorb anything. Of foods, fat is the only one ordinarily absorbed through the lymph channels, but there is not the least evidence that the superficial lymphatic glands have anything to do with this. The fat in the form of soap passes between the epithelial cells to the lacteals, which penetrate the villi, and are nowhere near the follicles and have no connection with them.

Russel H. Chittenten and Lafayette B. Mendel[3] say "there is some evidence that the lymphatic tissue elements are concerned in these synthetic transformations" (re-conversion of soaps into fats), but as the lacteals in the villi are surrounded by adenoid structure unconnected with the lymph follicles, it is the adenoid tissue in the villi that is more likely to be concerned than any other. Fat carrying leukocytes are found in the lacteals in the villi, but so far as I can learn they have never been observed in the lymph spaces surrounding the follicles, nor in other lymph spaces.

So that it seems so far we have no evidence that the superficial adenoid glands absorb anything during the digestive processes. Now if they are only capable of absorbing microörganisms, it would

[2] Ibid., p. 230.

[3] Ibid., i, 695.

seem that we should be better off without them. But by observing and studying their pathology some new light seems to be thrown on their functions, which will explain many things otherwise difficult to understand, such as McCallum's statement quoted above in regard to the invasion of the intestine by tubercle bacilli, that the tubercle nodules appear "sometimes in the lymphoid nodules or Peyer's patches."

Why is it that in diphtheria, scarlet fever, and other exanthemas the tonsils are often affected after other manifestations of the disease have been present for hours or days? This question first forcibly presented itself to me while I was attending a fellow-physician who, in opening a postscarlatinal abscess, received a scratch or prick on the dorsal surface of his right middle finger. The following day he performed an operation on another septic case, and while operating noticed discomfort in the finger. The following day the finger was worse and lymphangitis appeared on the forearm. On the fourth day he called me in. The finger was rather painful and moderately swollen, the swelling extending to the wrist. The red line of the lymphangitis reached the elbow. There was an enlarged and slightly tender anterior axillary gland; and slight fever and general malaise. He had himself freely incised the finger, and was treating it in approved antiseptic style. There was nothing wrong with the throat, nor any symptom of scarlet fever, which he had already had. About two days later the tonsil on the affected side (the right) became inflamed, and presented the typical appearance of scarlatinal tonsil. Two days afterward the left tonsil went through the same process. Convalescence was rather slow, but without notable incident. He himself examined a swabbing from the tonsils with the microscope to see if Loeffler's bacillus was present, but did not find it. Many staphylococci were present. I regret that no bacteriological cultures were made either from the pus from the finger or from the membrane in the throat. When first called I was rather surprised to find nothing apparently wrong in the throat, and was again surprised when the throat trouble appeared. Since the infection was both local and general when I first saw him, it appeared probable to me when the throat trouble developed that this was a form of elimination, like a diarrhœa as the result of an indigestion. The toxins or the toxins and the bacteria together were coming out through the tonsils thereby causing a local manifestation at their point of exit. It seemed that elimination was twofold: local, whereby the nearest tonsil was involved first, and general, whereby the other was involved secondarily. This seemed at first rather hypothetical, but in the light of further thought and observation it seems continually more probable, as explaining points otherwise obscure. Adopting this as a hypothesis, it explains the analogous condition of the solitary follicles and Peyer's patches in typhoid fever, a general and local infection (for the typhoid bacilli are probably absorbed

principally from the intestine) with elimination through the nearest superficial lymph glands. It explains the problem of tuberculous nodules in the lymph follicles in primary or secondary tuberculosis of the intestine. It explains the condition of the adenoid structures of the tongue in gastric and œsophageal diseases, of the pharynx in laryngeal affections, and in general the condition of chronic hypertrophy of these organs in all its forms.

It has been observed for years that tonsillar hypertrophy is not simply a local disease, but that the hypertrophy accompanies a diathetic taint or a condition of malnutrition; and that the removal of the hypertrophied organs often greatly benefits the general health is explained in two ways: First, the removal of a mechanical obstruction to respiration and deglutition, and, second, an improvement of the function of the tonsil, whose crypts and recesses have become so deeply situated that the normal outward flow is greatly impeded, and accumulations take place in them, to the detriment of the organ itself and of the whole body.

To some extent the different forms of hypertrophy may be regarded as indicating different forms of overstimulation. The hyperplastic form would indicate excessive elimination of some irritating substance from the general circulation, probably brought to the tonsil by the blood, and the true hypertrophic form would indicate local elimination, probably directly from the lymph space surrounding the tonsils, as in the case of nearby tuberculous disease. To some extent the true hypertrophy must be a compensatory condition, but nevertheless one requiring correction when excessive, as when the lacunæ are so deep that the eliminative function is interfered with.

The obscure relation between rheumatism and follicular tonsillitis will find its explanation in this hypothesis, rather than in the old belief that the rheumatism might enter through the tonsil. Some light ought to be thrown on the causes of appendicitis by this probable function of the adenoid structure in the appendix. Nor shall I be surprised if eventually some explanation along these lines may be found for gastric and duodenal ulcers and various other diseases of the digestive organs whose causes are still entirely obscure.

REVIEWS.

THE PROLONGATION OF LIFE; OPTIMISTIC STUDIES. By ELIE METCHNIKOFF. Eng ish translation by P. CHALMERS MIT HELL. Pp. 343. New York and London: G. P. Putnam's Sons, 1908.

SEVERAL years ago M. Metchnikoff's book, *The Nature of Man*, became known to the English-speaking public in its translation by Dr. Mitchell, and excited no little pleasure by its broad and pleasant philosophical views of life, and varied comment for its propositions concerning the limitation of human existence and the proposal to employ certain microbes to interfere with certain toxic influences which the author held as largely responsible for the appearance of senile changes of the body. The present volume is not precisely a sequel, but at least an elaboration, of the former book. Throughout the work, dealing mainly with the matter of senescence, its development, the question of natural death, and the propriety and means of its postponement in man, but also devoting attention, in a number of semidetached essays, to phases of individual and socialistic life, to the material side of morality, an analysis of pessimism, and to an illustrative discussion of the life of Goethe and an interpretation of his "Faust," there runs a thread of argument sustaining the value of human life to the individual as well as to the community, appealing to the recognition of an ideal or standard life cycle in which the end of existence must come with a sense of satiety, if not of pleasure, to the man who has run his race. The general line of his argument is well known: that, owing to a variety of circumstances of accident and disease, the life of man but rarely reaches its fullest measure of years, and that old age, while evasive of thorough analysis and appreciation, is premature to the most of us from the influences of toxins absorbed largely from putrefying material in our large bowel and from the activity of phagocytes with the higher cells thus influenced. The proposition to avoid such all-too-early changes by preventing putrefaction in the alimentary canal through the agency of lactic-acid producing organisms (notably the Bulgarian bacillus) ingested for the purpose, is likewise well known; it is further discussed in the volume, its value sustained by argument from analogies and from a small amount of illustrative but mainly incomplete experience.

One finds much to admire in the genial consideration of what is so widely regarded as a disaster and an anticlimax, the loss of power

and cessation which succeed the highest purposes and efforts of life, and in the author's deliberate ignoring of that infantile acceptance of stock-immortality for the real desideratum of personal con inuation which has become so much the vogue in scientific circles. As a materialist, he accepts the condition of life, but seeks to improve it and expand its usefulness; and his lines are not laid in the lamentations of failure and the hysteria of poetic revilement of the existing state, but in the practical efforts of a wisely persuaded man to recognize his limitations and to obtain all the good they permit. One recognizes well the personality of the illustrative case of "the man of science" whose development into the efficiency of contentment Metchnikoff draws with absorbing care in his study of pessimism and its relation to health and age, a tale adding sympathetic interest to the whole growth of the author's views and one suggesting, in its evolution, the possibility of further steps of hopefulness were the surroundings of the subject to permit. Orthobiosis, the normality of the life cycle, the author's desideratum, is perhaps chimerical, but none the less to be sought for and approximated. That even in the best regulation of life, age and death are sure to come, Metchnikoff does not seek to evade; but he speculates whether even normal sensescence and death may not, like age and death from disease, depend upon material causes whose principle may run through all species, an autointoxication comparable to the effects of disease, appearing in the close of the cycle and in some way connected with fulfilment of perpetuation of species. Be that as it may, human life, as we ordinarily estimate it, is, in the vast majority of instances, subject to the decaying and thanatizing influence of avoidable disease. Men rarely die of old age. They die (sometimes in old age) from violence, from the immediate effects of acute disease, and from the long-drawn influences of lesions induced by survived attacks, and from slowly advancing effects of poorly appreciated but almost ubiquitous and unnecessary faults of environment. One of these last, the bacteriologist Metchnikoff seeks in the putrefactive changes incident to the retention of putrescible waste in our large bowel, a part of the alimentary canal he traces in evolution by fancied necessities of our progenitors; and his proposition to prevent these changes by the introduction of antagonistic and apparently less harmful lactic-acid producing microörganisms is at least logical, even if as yet unproved beyond a suggestive degree. Taken merely as a part of a general truth, perhaps a very important part, it is not likely that serious denial of the author's ground will be urged; and none can more earnestly look forward, if the remedy succeed, to the measurable prolongation of efficient old age than practising physicians, whose bane of practice is in the effects of constipation and intestinal autointoxication.

In orthobiosis, in Metchnikoff's view, in orderly sequence of the life cycle not too seriously disturbed by adventitious factors, man

lives an ignorant and happy childhood, a violent and reckless youth, a sentient, appreciative manhood, and a deliberate, contented, and judicial old age—a childhood ignorant of death and its meaning, a youth reckless of death and the loss it entails, a manhood first sensing the real meaning of life and conservative of its possibilities, and an old age filled with the measure of accomplishment, wise to the faults which have harmed, and satisfied to relax the hold upon the cup. That pessimism and the embrace of *Weltschmerzen*, denial of life's joy in the overwhelming pain of disappointments, should be the natural portion of the young, of the poet, the artist, and the ill-balanced genius is no wonder to Metchnikoff, who sees in these subjects an absence of the sense of orientation, and an inability to acquire perfect adjustment because of the clashing of their overweening ambitions and ill-judged activities; and he is no admirer of the theory making for elimination of age for the advantage of the world in the strenuous life of the young. He has seen evidence, in the interim between the issue of *The Nature of Man* and that of the present volume, of the fate that would befall us were this the universal acceptance; and his philosophy promises in the orthobiotic cycle the conservation of energy from misapplication and its judicious apportionment to insure the greatest happiness to the individual and greatest advance to the state. It is almost a pity he does not extend his idea of toxic production of old age also to the explanation of no little proportion of the cases of pessimism he deems a not abnormal state of youth; calomel sweetens sour dispositions like a charm in many cases, has lifted a world of woes from melancholic poets, and has doubtless averted many a suicidal act.

Metchnikoff may be very correct in what he has written (the reviewer confesses his acceptance of much of the volume), and indeed, does not fasten himself to intestinal absorption as the sole source of our precocious age and death. He specifically insists in his discussion of a normal old age that there should have preceded it a normal life; it is this which is demanded in orthobiosis. Alcoholism and syphilis he urges as potent faults which hasten our end, and avoidable deteriorants are, of course, to be accepted as always to be eliminated if the normal end is to be expected. There might well have been written a chapter on the avoidable infections, which we treat too lightly from this point of view. An attack of scarlatina in childhood, apparently recovered from and not appreciated in the ordinary course of life, has, however, often left its sequel of potential failure under succeeding stress, and may well in after years, under influences which otherwise would be easily withstood, determine the development of a fatal nephritis. The summation of effects like these, each individual factor in itself perhaps trivial, may, with whatever care the man exert, determine the wearing out which comes in a seemingly inexplicable way. From this view, all infections should be avoided; and the total price for a group of post-

infectional immunities may involve the existence which their protection is relied upon to save. For the matter of that, what does normal senility and normal death amount to? Age and decay are with us from our prenatal period to the end, and much of our body is in continuous loss and replacement. It tallies with Metchnikoff's general view, but widens the view to the utmost, to think of the influences of cell upon cell in the cellular community we speak of as the human body and the harmonic equations which determine or permit the wasting and disappearance of the unuseful.

The natural death contemplated by Metchnikoff really does not occur, and theoretically has no reason for occurrence. If there were such a possibility as absolute orthobiosis there could be no materialistic reason for death. Yet natural death of cells does occur; the regular disappearance of the unuseful by atrophy cannot be doubted as commonly a natural process. It is here and in his inability to cope, whatever his suggestions, with the variations of life-limit seen among different species, that Metchnikoff virtually yields the incompleteness of materialistic views to explain the essence of life and practically acknowledges the predestination he distinctly denies in his pages. The book, however, was not written to defend the monistic theory of life, and it has well fulfilled its purpose of pointing out some material limitations to life; and it would be unfair and at the same time Quixotic to criticise it from this point of view. Yet, page for page, the essays on morality and the social life of man would grow in the optimism the author avows were there but the certain feeling that beyond it all there is a hope without justifiable denial by man that death, in whatever form it come, is not the end, but simply a stage in the evolution of an entity which manifests itself in our imperfect bodies in our present state, but which is not of the earth. A. J. S.

A Text-book of Human Physiology. Theoretical and Practical. By George V. N. Dearborn, A.M., Ph.D., M.D., Professor of Physiology in the Medical and Dental Schools of Tufts College, Boston. Pp. 550; 309 illustrations. Philadelphia and New York: Lea and Febiger, 1908.

Dr. Dearborn has prepared his *Text-book of Human Physiology*, as he states, primarily for medical and dental practitioners and students. In many respects the book follows conventional lines; that is, it comprises thirteen chapters—devoted to protoplasm and the cell, the nervous system, respiration, foods, digestion, nutrition, the blood and the lymph, the circulation, the skin, the senses, muscular action, mental function, and reproduction and development.

But the book is by no means a conventional volume; it contains much that is original, as well as novel—at least in presentation, and almost every page reflects the personality of the author, the enthusiasm of the successful teacher. As the author states in the preface, the book emphasizes the mechanism of the sense-organs, nerves, and muscles as the basis of the individual's efficiency, and it is the first text-book of medical physiology to recognize the more and more insistent demands of the mental process. The chapter on the mental functions is quite unusual in scope and manner of presentation, and well repays careful perusal; it should be read with much interest and profit by students and teachers of psychology and physical education. Special interest attaches also to the chapters on foods, digestion, and nutrition. Dietetic fads receive a well-merited share of condemnation, and emphasis is laid upon the importance of cookery—which is described as the art of preparing food for the pleasurable nourishment of man and other animals, and which is said, as much as anything else, biologically to differentiate man from his "poor relations," the brutes. The physiology of the circulation is well described, aside from the fact that the discussion of the myogenic, as contrasted with the neurogenic, theory of the cardiac activity is inadequate and altogether disappointing. Another of the noteworthy features of the book is the use of many original diagrams to illustrate divers physiological processes, such as cell metabolism, digestive processes, intestinal movements, the functions of the liver, glandular activity, urinary secretion, the functions of the blood capillaries, of the lymph capillaries, and of the skin, kinesthetic nerve impulses, muscular action, etc.; these, together with an appropriate explanation by the teacher, should materially assist the student easily to acquire a knowledge of physiological problems. There is an appendix, of seventy pages, containing directions for performing certain fundamental physiological experiments, with brief theoretical notes; a list of topics suitable for essays and conference discussion; and conversion tables of various sorts—all of which render the book valuable as a laboratory manual.

The book may be cordially recommended: it is of moderate size; it is original; it contains the essential facts of physiology set forth clearly, concisely, and perhaps somewhat dogmatically (which in a book of its kind is by no means a defect); it accentuates matters of prime importance, those of secondary rank being merely mentioned or perhaps omitted; and it frequently contrasts physiological phenomena with related aspects of practical medicine. A. K.

AN INDEX OF TREATMENT. By VARIOUS WRITERS. Edited by ROBERT HUTCHISON, M.D., F.R.C.P., Physician to the London Hospital, and H. STANSFIELD COLLIER, F.R.C.S., Surgeon to St. Mary's Hospital, London. Revised to conform with American Usage by Warren Coleman, M.D., Professor of Clinical Medicine in the Cornell University Medical College, New York. Pp. 888. New York: William Wood and Co., 1908.

THE TREATMENT OF INTERNAL DISEASES. By NORBERT ORTNER, M.D., of the University of Vienna. Edited by NATHANIEL BOWDITCH POTTER, M.D., Instructor in Medicine in Columbia University, New York. Translated from the Fourth German edition by FREDERICK H. BARTLETT, M.D. Pp. 658. Philadelphia and London: J. B. Lippincott Co., 1908.

THE TREATMENT OF DISEASE. By REYNOLD WEBB WILCOX, M.D., Professor of Medicine in the New York Postgraduate Medical School. Second edition. Pp. 932. Philadelphia: P. Blakiston's Son and Co., 1908.

THE existence of what is sometimes referred to as a revival of interest in therapeutics is well attested by the recent publication of several books devoted more or less exclusively to the subject; of these, the three at present under notice may be considered representative. The *Index of Treatment*, the combined work of some seventy contributors, reflects the advanced teaching and practice of the best English schools; and it has been adapted to the requirements of practitioners in this country by the association of a capable American editor. The majority of the contributors are well known and well qualified to write on the topics that have been assigned them; some even have attained to international reputation. Designed for the practitioner, the treatment discussed is largely medical, but surgical measures have not been entirely ignored; there is, for instance, some good, albeit conservative, advice in regard to the surgical treatment of borderland diseases, such as appendicitis, cholelithiasis, gastric ulcer, etc., although little is said regarding the aberrant phenomena of gallstones or ulcer of the stomach. The work as a whole, however, is of undoubted value, since four editions have been issued in England within a year.

Ortner's *Treatment of Internal Diseases* has achieved a notable success among the German-speaking peoples. In general it reflects the best therapeutic practice of Germany and Austria, although it is quite personal in its tone. There is some mention of pathological physiology as it bears on treatment; and in addition to drug therapy, emphasis is laid upon the importance of mechanical, dietetic, climatic, hydrotherapeutic, and other extramedicinal methods. The value of the book and its adaptability to English-speaking practitioners has been much enchanced by the careful and judicious work of the American editor.

The nature and scope of Wilcox's *Treatment of Disease* is best represented in its subsidiary title, a *Manual of Practical Medicine;* it is, in fact, a manual of medicine in which an unusual share of attention has been devoted to methods of treatment. Many readers will note with ill-disguised concern a certain fondness for divers proprietary remedies; and here and there there is some lapse from the approved practice of many leading American physicians: thus, in the treatment of pneumonia, although creosote carbonate is recommended as a means of limiting the infection, and oxygen is said to be of value, there is no mention of the importance of fresh air (aside from advising a well-ventilated room to be kept at a temperature of 65° to 70°). The value of fresh air is commented upon by the American editor of Ortner's book, but no mention of it occurs in the *Index of Treatment.* In general, however, one may say that Wilcox's book is eminently good, practical, and to the point. A. K.

MEDICAL GYNECOLOGY. By SAMUEL WYLLIS BANDLER, M.D., Adjunct Professor of Diseases of Women in the New York Postgraduate School and Hospital. Pp. 676; 135 illustrations. Philadelphia and London: W. B. Saunders Company, 1908.

THE advances of the operative possibilities in the treatment of the diseases of women during the last two decades have created an undoubted tendency to belittle the importance of many conditions which either are not indications for operative intervention, or which may be quite as well treated by non-operative means. It is, therefore, a matter of congratulation that books of this nature are making their appearance. It of course goes without saying that many cases which demand operation are even now treated without operation either through the ignorance of the medical man or from an even less excusable cause; this book will aid in instructing ignorance; it cannot be expected to teach morality also. The present volume opens with a good chapter of forty-seven pages upon the gynecological examination. As our only criticism of this portion, we would suggest that it is the experience of most of us that one finger is better than two, as a rule, in vaginal or bimanual examinations. We are very glad to find that the cystoscope perfected by Tilden Brown is figured and advocated, as it will render the examination much simpler to the ordinary operator than some of the models recommended in recent books. Next in order is a section of a little less than 100 pages devoted to the methods employed in medical treatment. Under this heading are included, among others, the indications for the use of electricity, pelvic massage, pessaries, and intra-uterine therapy. With regard to the latter,

we are glad to note that while directions are given for its performance, its dangers are strongly enforced. We wish that the half-hearted justification of the use of the sound or stem pessary, as a diagnostic measure in the determination of cervical stenosis as a cause of dysmenorrhea, had been instead a hearty condemnation. The remainder of the volume is taken up by the consideration of the various pathological conditions included within the domain of gynecology. The directions regarding treatment are definite and the symptomatology is clear. We are glad to note that recourse to operative relief is always advised when conditions demand it. In the consideration of the treatment of inevitable abortion, we are sorry to see that the old method of dilatation of the cervix by gauze packs is still given a place, as it certainly seems to us that anyone who can be trusted to pack a uterus, and, if need be, to repeat that packing some hours later, and then remove the product of conception by the forceps or finger, might certainly be considered competent to use the steel dilators, thus avoiding septic infection without, to our mind, any increased risk from instrumentation over the method referred to. We particularly appreciate his treatment of sterility, because of the general fairness of presentation and definiteness in directions; particularly to be praised are his negations as to curettage in this condition.

There is a very satisfactory chapter upon gonorrhœa, special attention being called to the frequency of gonorrhœa without clinical signs. While the author gives the various procedures sanctioned by different authorities for the treatment of intra-uterine Neisserian infection, we are glad to note his own personal avoidance of these manipulations, and also his definite warnings with regard to them. In discussing the question of retrodisplacements of the uterus, the author states his belief that an uncomplicated case of retrodisplacement does not in itself cause symptoms, but that they are due to other associated conditions, standing in no direct relation to the retroflexion. We are especially glad to note his favorable opinion of the pessary and ergot after delivery in cases of displacement. In the chapter following upon uterine subinvolution the author gives directions as to the care of the puerperal patient, which, although possibly a little more radical than we would ourselves favor, are, nevertheless, a step in the right direction; we have long favored the early change of position from the supine to the lateral and prone, but have never been able to convince ourselves that the use of the commode as early as the fifth day is entirely free from danger.

The book can be most heartily recommended to the profession. One of its most praiseworthy characteristics is the conservative spirit which pervades it; this, as may be inferred from the opening paragraph of this review, is, in our opinion, a matter for congratulation.

W. R. N.

ESTIMATION OF THE RENAL FUNCTION IN URINARY SURGERY. By J. W. THOMSON WALKER, M.B., C.M. (EDIN.), F.R.C.S., Hunterian Professor of Surgery and Pathology, Royal College of Surgeons of England (1907). Pp. 295; 75 illustrations. London and New York: Cassell & Co., Ltd., 1908.

DR. WALKER's book comprises a clinical study of the means of estimating the renal function in surgical diseases of the urinary organs. Part I is concerned with the estimation of the total renal function, and Part II with that of the function of one kidney. Attention is given to the older methods of renal analysis, such as the chemical and microscopic study of the urine; in addition, the significance of cryoscopy, of the electrical resistance of the urine and the blood, of the surface tension of the urine, and of the elimination of certain chemical substances by the kidneys are discussed in detail and judicially. The methylene blue test is believed to be more trustworthy than the quantitative examination of the urea or the appearance of general symptoms of renal inadequancy, especially in the more severe grades of kidney disease. The phloridzin test also is considered to be of value, since a diminished phloridzin glycosuria is said to indicate a depressed renal function which is usually due to disease of the kidney, and a complete absence of sugar should be regarded as a sign of advanced renal lesion. The technique of these and other tests, as well as of divers surgical procedures resorted to in investigating the urinary organs, is fully described. The value of the book is much enhanced by the incorporation of many illustrative cases that form the basis of the conclusions deduced. The book should prove of much value, not only to surgeons, for whom it is intended primarily, but also to general practitioners. A. K.

L'APHASIE DE BROCA. By DR. FRANÇOIS MOUTIER. From the Laboratory of Prof. Pierre Marie (Hospice de Bicêtre). Pp. 769; 175 illustrations. Paris: G. Steinheil, 1908.

THE author, a student of Prof. Marie, in an excellent presentation of 769 pages, again brings up the discussion of aphasia. He begins with a short introduction of the causes of the controversy, and in the first part of the book gives an excellent historical resume of the subject. In the second part is taken up the cortical localization of Broca's aphasia. The author attempts to show that the old or classical view of Broca's aphasia is based upon a fallacy. In a resume of the literature up to the present time he comes to the conclusion that there is no evidence that Broca's aphasia results from isolated disturbances of the third frontal convolution. He quotes

84 negative cases in which Broca's aphasia was present in 57, with no lesion in the third frontal convolution, and 27 cases in which there was no aphasia and yet there was a lesion of the third frontal convolution. In the third division the nature and clinical symptoms of Broca's aphasia are discussed. He reiterates the view advanced by Marie that there is no such thing as motor or sensory aphasia, but that aphasia is a disturbance of the intelligence generally, and principally of that concerned with speech. By the first he means a disturbance in attention, memory, and mimicry; and by the second, a disturbance of understanding and of speech, as illustrated in writing and reading. He then discusses the mental disturbances occurring in aphasia, and concerns himself with word pictures of motor, acoustic, and visual origin, to which he is antagonistic. In the last part of the book there is presented a study of 44 cases of aphasia. In 24 of these the brain was examined, and in one-half serial sections were made. It would be impossible in a review of this kind to give the results of this excellent work, but it might be noted that there were 3 cases with disturbance of the third frontal convolution without aphasia, 4 cases with anarthria, or Broca's aphasia, without a lesion of the third frontal, while in 8 there was anarthria in 1, with a lesion of the third frontal and Marie's zone. Of course, the object of this work is to further Marie's views, and it is well done. At the same time, it must be remembered that throughout there is an evident attempt to justify these views without, perhaps, critical attention being paid to the opposing view. On the whole, the work is well done, and should be read by everyone interested in the question of aphasia. T. H. W.

A Manual of Obstetrical Technique as Applied to Private Practice: with a Chapter on Abortion, Premature Labor, and Curettage. By Joseph Brown Cooke, M.D., Adjunct Professor of Obstetrics in the New York Polyclinic Medical School and Hospital. Sixth edition. Pp. 254. Philadelphia and London: J. B. Lippincott Co., 1908.

The author's idea in preparing this little book has been to give detailed instruction to the younger members of the profession, in their early work among the poor, in regard to the best methods by which they may approximate the hospital technique of the present day. He undoubtedly takes the only tenable ground when, in his preface to an earlier edition, he inveighs against the inferior work too often excused upon the ground of an inadequate fee. The instructions given are definite, the whole subject is satisfactorily covered, and there are but few points with which one may feel inclined to differ. It is, for instance, hardly sufficient to examine the urine

once a month up to the eighth month, as suggested by the author. We cannot see the value of any attempt at urea estimation among the poorer class, since any attempt to estimate the intake of the nitrogen would be worse than useless. Furthermore, the advice that with a conjugate of 8 cm. labor should be induced at the thirty-sixth week and the delivery aided by forceps or version, with the alternative of induction at the thirty-second week and the subsequent use of the incubator, is hardly the attitude of the modern obstetrical specialist. It is true that the book was not prepared for the expert, but since, in the present day, there are men in every town competent to handle major operative obstetrics, there does not seem sufficient reason to advocate such methods. If the beginner were more thoroughly trained in methods of diagnosis, in order that he might know when to summon help, there would be a great improvement in both the mortality and morbidity of childbed. There is no question, in the minds of the majority of obstetrical operators that the use of rubber gloves is an added safeguard in the technique of delivery, and, therefore, it seems that their advantages might have been more definitely insisted upon. It is true they are included in the very complete armamentarium advised by the author, but their use is not insisted upon.

Aside from the above mentioned differences of opinion there is nothing to which exception can be taken, and there are very many most excellent features in the volume. Among the points to which the attention of the younger practitioner may well be directed, is the statement that eclampsia is an absolutely preventable disease provided the patient places herself unreservedly under the care of the physician, and that the "basiotribe is as far beyond the craniocast as the railway train is beyond the stage coach." Both these statements if heeded will tend to decrease the difficulties of practical obstetrics, though we are a little doubtful about the advisability of too easy access to the latter instrument as advocated by the author. We feel that a careful reading of the volume will well repay not only the obstetric tyro, but also many a man of considerable experience.

W. R. N.

TEXT-BOOK OF DISEASES OF THE NOSE, THROAT, AND EAR. By FRANCIS R. PACKARD, M.D., Professor of Diseases of the Nose and Throat in the Philadelphia Polyclinic College for Graduates in Medicine. Pp. 369; 138 illustrations. Philadelphia and London: J. B. Lippincott Co., 1909.

FOR the use of students and general practitioners the work before us comprises, it is likely, as fair a summary as can be selected of such diseases of the nose, throat, and ear as are likely to come under the

cognizance and permanent care of the general practitioner. To these are added a few conditions which pertain rather to the domain of the skilled specialist or the unusually skilled general surgeon: mainly the radical procedures for advanced diseases of the accessory sinuses of the nasal passages, and for mastoid operations on the ear. Of the 350 pages devoted to the text, 37 are applied to descriptions and illustrations of the instruments required, and the methods employed for routine examination and treatment, and to remedies and the methods of their application. A scant 100 are devoted to the anatomy and diseases of the ear, malformations of the auricle being very copiously illustrated. Of the 200 odd pages devoted to the anatomy and diseases of the nose, rhinopharynx, pharynx, and larynx, but 20 are occupied with diseases of the larynx.

The teaching throughout is admirable. The illustrations with a few exceptions are excellent, especially the anatomical ones and most of the skiagraphic series. Many of them are new and superior in selection and execution. The language is good and to the point. Students are frequently cautioned against reliance on popular remedies, on the abuse of cocaine, and on the overlust for operative interference. Old established methods of treatment are not discredited. Thus, in discussing remedies for topical applications the long-established value of the too much neglected silver nitrate is fully appreciated; and in discussing minor operative procedures, even the too much despised tonsillotome is advocated in no uncertain terms as the preferable instrument in many cases in which it is often discarded, at least in the hands of the inexperienced operator; and Sajous' snare is appreciatively commended in attacks upon nasal polyps. In describing operative procedures, the accidents possible in execution or in sequence are not ignored; but care is taken to indicate measures for prevention and for control in emergency. Subjects recently brought into additional prominence are discussed, especially diseases of the eye following pathological conditions in the nose and the accessory sinuses. J. S. C.

SURGICAL MEMOIRS AND OTHER ESSAYS. By JAMES G. MUMFORD, M.D., Instructor in Surgery in the Harvard Medical School, Boston. New York; Moffat, Yard & Co., 1908.

DR. MUMFORD, whose ability as an interesting writer on medical history has already been proved by his entertaining *Narrative of American Medicine*, has in this volume collected a series of addresses which he has delivered from time to time, together with some of his previously published articles, and out of the whole has evolved a

most agreeable book. The essays on the surgeons of the eighteenth and early nineteenth century are very interesting, particularly those on John Hunter, Sir Astley Cooper, Sir Benjamin Brodie, and John Collins Warren. Although the facts he presents are mostly gathered from the previously published biographies of these worthies, they are retold in such a graphic and pleasing manner that they acquire an original flavor. The essay on "The Teachings of the Old Surgeons" is a really valuable summary of the state of surgical knowledge in the times of various surgeons, from Guy de Chauliac to Baron Larrey. Dr. Mumford possesses the happy faculty of getting at the gist of his subject and dressing it out in a concise and forceful style which compels attention and carries the reader along. He recalls the achievements of the past masters of the art of surgery, and shows us that in surgery, as in all other human pursuits, much that we deem modern was in reality known and taught many years since. This is the kind of book which if placed in the hands of medical students or young practitioners cannot fail to do much good. Its pages are a stimulus to good work, and at the same time cause the reader to see that success can only be achieved in the profession by self-sacrifice and devotion to high ideals.

F. R. P.

THE PATHOLOGY OF THE EYE. By J. HERBERT PARSONS, B.S., D.S.C. (London), F.R.C.S. (England), Assistant Ophthalmic Surgeon to the University College Hospital, London. Volume IV, General Pathology. Part II, pp. 298. New York: G. P. Putnam's Sons. London: Henry Frowde, Hodder & Stoughton, 1908.

THIS, the concluding volume of Parsons' monumental work, is perhaps the most interesting of the whole to the ordinary reader, being less what may be termed specialized. Its subject matter consists of an exhaustive account of injuries with sympathetic ophthalmia, and panophthalmitis, enophthalmos and exophthalmos, disease of the orbit and symptomatic diseases of the eye; that is, occular diseases dependent upon general affections and diseases of other organs. A short chapter upon heredity closes the work. Each article is richly documented and testifies to a most extensive reading. Upon controverted points Parsons has positive opinions and states them with the reasons therefore after exhaustive statement and criticism of rival views.

Regarding the pathogenesis of sympathetic ophthalmia, after detailing the various hypotheses as classified by Schirmer, he gives the preference to the bacterial metastatic theory, and in this we believe he is in accord with the trend of authority. The advance of

bacteriology during the last few years has weakened the force of the objections which Leber and his followers have urged against it. The intra-ocular signs of general arteriosclerosis so strongly insisted on by Gunn and others are made more intelligible by a number of illustrations. A brief reference is made to the occurrence of Mikulicz's disease; that is, symmetrical enlargement of the lacrimal and salivary glands, but its pathology is not discussed.

Each additional volume as it appeared has strengthened the conviction that this work is to be the standard for years to come upon the pathology of the eye in English. Heretofore the seeker for information upon this subject has been compelled to have recourse to books written in foreign languages, especially German. The entire profession, and not the ophthalmologists alone, will undoubtedly receive with thankfulness a work which so ably and exhaustively puts its reader in possession of the latest views in the rapidly growing field of pathology, which find such striking illustration in the various tissues which enter into the organ of vision. T. B. S.

CATARACT EXTRACTION. BEING A SERIES OF PAPERS WITH DISCUSSION AND COMMENTS READ BEFORE THE OPHTHALMOLOGICAL SECTION OF THE NEW YORK ACADEMY OF MEDICINE, 1907–1908. Edited by J. HERBERT CLAIBORNE, M.D., formerly Adjunct Professor of Ophthalmology in the New York Polyclinic. Pp. 169. New York: William Wood & Company, 1908.

THIS symposium upon cataract extraction by twelve New York ophthalmologists is a fair resume of the present status of the operation. While the opinions vary somewhat regarding details, there is a fair unanimity upon all essential points except upon the question of the simple or combined method. The pendulum is now swinging in the direction of the latter. The 8.61 per cent. of prolapses are the stumbling block in the way of many an operator who would otherwise decide in favor of simple extraction. We confess to some surprise at the statement by some of the participants that the latter is the easier method. Claiborne advocates extraction with a lance-shaped keratome of his devising and also describes a new instrument to scratch the capsule for artificial maturation. The incisions are so fine that the aqueous humor is brought in contact with the lens substance without protrusion of the latter. Lambert contributes a paper upon removal of the lens in high myopia, with a report of two highly successful cases in young women, but does not advocate the practice in all cases of high myopia. The editor justly observes that the operation will probably never be generally employed in this country. Indeed the editor's summing up at the conclusion of each paper is always judicious and interesting. T. B. S.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Sterile Serous Effusions with Empyema and Lung Abscess.—KÖNIGER (*Münch. med. Woch.*, 1909, lvi, 603) mentions the occurrence of multilocular tuberculous pleural effusions, the exudates being walled off and separated from one another. Such a condition is much rarer in acute infections. It is not a very unusual experience in making exploratory puncture to find a thin, clear, serous exudate at one point, a purulent fluid at another. This has usually been attributed to the settling of the cellular elements in the exudate. Studying a number of cases bacteriologically and cytologically, the author has found that the purulent fluid contains microörganisms, while the serous is usually sterile. From observations made on a number of cases, he concludes: (1) That acute pleuritic empyema which becomes encapsulated early, not infrequently leads to extensive serous effusion in the adjacent part of the pleura, which ordinarily does not communicate with the primarily infected area. (2) That such a serous effusion is sterile and is quite rich in cells, the majority of which are polymorphonuclear neutrophiles, with a few lymphocytes, endothelial cells, etc. The cells are very well preserved, few of them showing the degenerative changes seen in the pus cells of the purulent exudate. (3) Bacteriologically and cytologically the findings show that the difference in the fluids at the two points does not result from settling of the cells. The serous effusions probably owe their origin to bacterial toxins and are comparable to the œdema surrounding a phlegmon in the tissues. (4) Similar serous effusions arise in connection with purulent processes in the lung (abscess, gangrene) as well as with other severe suppurations in the neighborhood of the pleura (subphrenic abscess, liver abscess). (5) All the above

mentioned serous exudates have this in common, that they are caused by a localized infection. Their clinical importance lies in the fact that their presence renders much more difficult the recognition of a suppurative process; they are apt to confuse the diagnostician because of their comparatively harmless appearance and their sterility. The cytological examination combined with the bacteriological finding may, however, raise one's suspicion.

The Excretion of Hexamethylenamin (Urotropin) in the Cerebrospinal Fluid, and its Therapeutic Value in Meningitis.—Crowe (*Johns Hopkins Hosp. Bull.*, 1908, xix, 109) first studied the excretion of urotropin in the bile and pancreatic juice in the report a year ago, and he recorded a case of purulent meningitis following a postoperative cerebrospinal fistula which cleared up in three weeks from the administration of urotropin by the mouth. Since then (*Ibid.*, 1909, xx, 102) he has demonstrated that the urotropin which is administered by the mouth in man, rabbits, and dogs invariably appears in the cerebrospinal fluid, a maximum amount in from thirty minutes to one hour after ingestion. In therapeutic doses an amount appears sufficient to exercise a decided inhibitory effect upon the growth of organisms inoculated into the spinal fluid after its removal from the body. Sixty to eighty grains a day in dogs and rabbits will either defer or prevent the onset of a fatal, experimental streptococcic meningitis. In view of these observations he advises its application as a prophylaxis in all clinical cases in which meningitis is a possible or threatened complication, such as fractures of the skull, operations upon and infections of the nasal sinuses and middle ear; even after simple lumbar puncture. Thirty to sixty grains a day may be given.

Toxic Effects from Bismuth Subnitrate.—Beck (*New York Med. Jour.*, 1909, lxxxix, 16) reports seven cases from the literature, in addition to his own experience, with poisoning from bismuth subnitrate. The clinical picture is one of collapse with cyanosis, vomiting, diarrhœa, and abdominal cramps. Böhme has shown that these are symptoms of gastro-enteritis and methemoglobinemia due to acute nitrite poisoning arising from the conversion of the subnitrate into nitrite in the large intestine by bacterial action. Beck points out that bismuth subnitrate is used freely and regarded as harmless, especially by radiographers. In conclusion, he states that small doses by the mouth are harmless. In larger doses sufficient nitrites are liberated and absorbed to produce an acute nitrite poisoning, characterized by methemoglobinemia and collapse. This may terminate fatally. Children and individuals suffering with intestinal putrefaction are very susceptible. This acute nitrite poisoning is a distinct and separate affection from the more chronic bismuth absorption. Beck advises the use of some other salt of bismuth than the nitrate. He finds that iodine neutralizes the nitrite in acute poisoning, whereas alcohol and glycerin hasten its liberation.

The Recognition of Glycuronic Acid in the Urine.—C. Tollens (*Münch. med. Woch.*, 1909, lvi, 652) recognizes the need for a simple test for the recognition of glycuronic acid in the urine. He points out that it is increased after the administration of various drugs, such as phenol,

salicylic acid, chloral hydrate, cresote, camphor, morphine, etc., and this increase may be of assistance in the diagnosis of poisoning with any of these. Furthermore, patients presenting an increase of the paired glycuronic-acid compounds have been looked upon as diabetics and have been refused life insurance, because their urines reduce copper solutions. Again, it has been shown that aromatic substances arising in deep-seated, unrecognized abscesses may become paired with glycuronic acid and thus lead to its increase in the urine. Hoppe-Seyler has demonstrated that excessive intestinal putrefaction may give rise to large amounts of indoxyl-glycuronic acid in the urine. It is evident, therefore, that the recognition of increased quantities of glycuronic acid compounds in the urine may be of aid in a variety of conditions. Of the tests for glycuronic acid in the urine, the orcin test is not reliable, for pentoses also give it. B. Tollens has devised a test which is simple, quite accurate, and easily carried out. It is based on the fact that naphthoresorcin and HCl, when acting on glycuronic acid, give rise to a blue pigment, *soluble* in ether, which produces a well-marked, dark band in the sodium line on spectroscopic examination. The pigments formed in this reaction with pentoses and various sugars are *insoluble* in ether. Method: To 5 c.c. of urine add a bit of naphthoresorcin about the size of a millet seed and 5 c.c. of fuming HCl (sp. gr., 1.190). Heat to boiling over the flame and continue boiling gently for one minute. Now allow the test-tube to stand four minutes and then cool in running water. Add an equal volume of ether, shake vigorously, and set aside till the ether is clear. (The clearing is hastened by the addition of a few drops of alcohol.) If paired glycuronic acid compounds are present in excess, the ether extract is dark blue to violet, while small amounts produce a faint bluish or reddish violet color. Examined spectroscopically, the ethereal extract shows a single dark band near the sodium line. Instead of napthoresorcin in substance, one may employ 0.5 c.c. of a 1 per cent. alcoholic solution. The test, performed as above, is delicate enough to detect the small quantities of glycuronic acid present in normal urine. With large amounts of glycuronic acid it may be necessary to dilute the ether extract before spectroscopic examination. From the intensity of the reaction one may make a rough estimate of the quantity of glycuronic acid present.

Functional Test of the Pancreas.—Gross (*Deut. med. Woch.*, 1909, xxxv, 706) has devised a method for estimating quantitatively the trypsin in the feces. The method is based on the fact that casein rendered soluble in alkali is precipitated on the addition of acetic acid, while the products of its digestion remain in solution. For fecal examination one dissolves 0.5 gm. of caseinum purissimum (Grübler) in one liter of 1 to 1000 soda solution, warming moderately. The feces to be examined are rubbed up in a mortar with three times the quantity of 1 to 1000 solution of soda until a homogeneous suspension is obtained, and then filtered until the filtrate is clear. (Usually this is very quickly accomplished, but if bacteria cause the turbidity, they will settle to the bottom in a short time and the clear fluid may be decanted.) 100 c.c. of the casein solution is placed in a flask and 10 c.c. of the fecal suspension added. The mixture is shaken, placed in an incubator at 38° to 40° C. and from time to time small quantities are withdrawn

and tested with 1 per cent. acetic acid until a precipitate no longer occurs. Employing this technique over 200 stools from patients without demonstrable pancreatic disease were examined, and a proteolytic ferment was found in all. A few drops of chloroform was added to prevent bacterial growth and the probability that the ferment was trypsin was further shown by the lack of digestion after the addition of 0.5 c.c. of human blood serum (antitrypsin). Erepsin was practically excluded by removing the pancreas of dogs. Feces from such animals failed to digest the casein. Of the 200 cases the duration of digestion until complete was eight to thirty hours. The rapidity of digestion and, therefore, the amount of trypsin were found to vary with the variety of food given the patient. Digestion was most rapid after proteid, next after fat, and slowest after carbohydrate food. Therefore, the examination is more satisfactory after proteid nourishment, and here the average time required for complete digestion is twelve to fourteen hours (limits eight to fifteen hours). In various intestinal diseases Gross found normal tryptic digestion, except that in diarrhœa the casein is digested more rapidly. In one patient with complete closure of the ductus choledochus no tryptic digestion was demonstrable. A similar result was obtained in a case of cancer of the pancreas and in this case absence of pancreatic juice was the only definite sign of pancreatic disease. In a patient with cirrhosis of the pancreas and a clinical picture of pernicious anemia normal tryptic digestion occurred.

Thymol as a Source of Error in Heller's Test for Urinary Protein.—Weinberger (*Proc. Soc. Exper. Biol. and Med.*, 1908, vi, 4; *Jour. Amer. Med. Assoc.*, 1909, lii, 1310) considers the sources of error in Heller's nitric acid test for urinary proteins. In urines concentrated beyond a certain degree the test will fail even in the presence of large amounts of albumin. According to Kenny, too much formaldehyde used in preserving the urine will render the test unreliable. In the course of other investigations Weinberger found that thymol also as a preservative was a source of error. If such a urine is floated upon concentrated nitric acid, there forms precisely at the time of junction a grayish white ring 0.5 mm. high, resembling the ring given by a faint trace of albumin. In an excess of urine the cloud will not disappear on shaking. Warming will not prevent the formation of the ring—if anything, will make the reaction more distinct. Dilution of the urine with three or four times its volume of water has no prohibiting effect. It occurs in both acid and alkaline thymolized urines, more pronounced in the latter. In urine containing both albumin and thymol in various amounts each ring may be discerned. The albumin ring is wider and white; whereas, the thymol ring forms underneath it and is gray and thin. However, the albumin ring may be completely covered by the latter. The necessary modification is the removal of the thymol by extraction with an equal volume of petroleum ether. On the other hand, ether will not extract the thymol when it has been given internally and is excreted through the kidneys, a point of some importance.

A New Method for Finding Tubercle Bacilli.—Lange and Nitsche (*Deut. med. Woch.*, 1909, xxxv, 435) have described a new method for the examination of sputum for tubercle bacilli. If a pure culutre of

tubercle bacilli in a watery medium be mixed with a culture of non-acid fast bacilli, the two can be separated almost quantitatively by the use of a hydrocarbon, the tubercle bacilli being found in the latter. This fact has been applied to the examination of sputum, urine, pus, etc. Sputum should be rendered homogeneous. The choice of the hydrocarbon is of some moment. Petroleum ether, benzine, ligroin, toluol, and xylol have proved satisfactory. The best results are obtained, however, with ligroin of a boiling point of 90° to 120° C. It has the advantage of being cheap. The specific gravity of the hydrocarbon should not be too much below 1; otherwise it rises too quickly after shaking. The advantage of the low boiling point is that the reagent quickly evaporates and does not interfere with subsequent fixation of the preparation. There is also less tendency for the drop to "run" when evaporation is rapid. To render the sputum homogeneous the authors recommend normal potassium hydrate as the most satisfactory reagent; 5 c.c. of sputum and 50 c.c. of normal potassium hydrate are well shaken and allowed to stand three hours at a room temperature (shorter in incubator at 37°); repeated shaking hastens the solution; 50 c.c. of tap water and 5 c.c. of ligroin are added and the whole shaken vigorously, preferably in a stoppered graduated cylinder. The separation of the hydrocarbon requires several hours, but warming the emulsion to 65° greatly facilitates this. When the separation is complete, the tubercle bacilli will be found at the bottom of the clear layer of ligroin. Employing this technique the authors have been able to find many tubercle bacilli in sputum which appeared free of them when examined in the usual way. Furthermore, in their preparations there was a striking absence of bacteria.

Iron as a Substitute for Bismuth in Radiography.—TAEGE (*Münch. med. Woch.*, 1909, lvi, 758) confirms the findings of Lewin that iron may be substituted for bismuth in radiographic work. Two advantages are possessed by the iron: (1) Apparently there is no danger of intoxication, as may happen after using bismuth; and (2) it is much cheaper, costing about one-thirteenth as much as the bismuth. The preparation, which he has found most satisfactory, is red oxydate of iron (*German Pharmacopœia*). Of this Taege himself has taken 50 grams without any perceptible effect.

The "Pulsometer."—FELLNER (*Deut. med. Woch.*, 1909, xxxv, 211) has discovered a method for determining the rate of flow of the blood in man, the results of which correspond with those previously determined. in animal experiments. An Esmarch bandage is applied to the arm to remove the blood from the capillaries and veins. The cuff of the sphygmomanometer is now applied to the arm at the upper end of the bandage. The pressure is raised 30 to 50 mm. Hg. above the systolic pressure and the bandage then removed. A stop watch which registers 0.2 of a second is now started and simultaneously the pressure on the sphygmomanometer is released. The arm is pale and (before releasing the pressure) pulseless. The fingers are observed, and at the first sign of reddening in them the watch is stopped. The distance is measured and the time is read off on the watch. About 1000 experiments on healthy and diseased persons gave a velocity of 200 to 400 mm. per

second. Fellner has devised an apparatus which he says is especially suited to this procedure.

A Skin Reaction in Carcinoma from the Subcutaneous Injection of Human Red Blood Cells.—Elsberg (*Proc. Soc. Exper. Biol. and Med.*, 1909, vi, 91; *Jour. Amer. Med. Assoc.*, 1909, lii, 1310) attempted to produce a specific hemolytic reaction locally by the injection of red blood cells under the skin of a carcinoma patient. He was led to these experiments by the recent demonstration that hemolysis occurs when the blood serum of a patient suffering from carcinoma is mixed with normal human red blood cells. The technique employed was simple. Blood was obtained aseptically from normal individuals, preferably children, and defibrinated. A 20 per cent. emulsion of the washed red blood corpuscles was used, five minims of this being injected subcutaneously in the anterior surface of the forearm. A "positive reaction" consisted of infiltration, tenderness, and redness at the site of injection, in six to eighteen hours. Simple discoloration or the puncture wound was all that was seen in the negative cases. Thirty-four injections were given to 20 cases of known carcinoma, and every one of the cases had a positive reaction; of four cases with known sarcoma; three gave a positive reaction. The reaction was negative in all but 3 of 100 individuals who were either normal or suffering from such diseases as nephritis, leukemia, syphilis, benign tumors, tuberculosis of the lungs, bladder, and kidneys, and many acute and chronic inflammatory conditions. No reaction was obtained in several patients in whom malignant disease was suspected but not found at operation. An exploratory incision has confirmed the positive reaction in several patients in whom carcinoma was not suspected. The injection of laked bood caused a positive reaction in all patients, whether suffering from malignant disease or not. This seemed to show that the positive reaction in carcinoma from blood cell injection was due to hemolysis. It may prove that this is constant enough to be a characteristic and easily recognized aid to diagnosis.

SURGERY.

UNDER THE CHARGE OF

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A Modification of the Bassini Operation, Especially in Large Herniæ.—Caminiti (*Zentralbl. f. Chir.*, 1909, xxxvi, 244) makes an incision through the skin and external oblique muscle, opening the inguinal canal. The fibers of the cremaster are then separated and the sac of the hernia

exposed and isolated from the surrounding tissues The separated and, emptied sac is then ligated at its neck and the stump first fixed above or the operation carried further toward its completion. Instead of now taking up together in one bundle, the cord, the common tunica vaginalis, and cremaster, they are separated from one another, and the elements of the cord carefully isolated. Temporarily these are kept together by wrapping them with the cremaster in gauze. If the stump of the cord has not already been drawn upward and fixed in the upper part of the wound this is now done. The internal oblique and transversalis muscles are then sutured to Poupart's ligament. The peripheral edge of the cremaster is removed, so that only its compact portion remains. It is then sutured over the other layers. The cord structures are then spread out over this layer. The external oblique is sutured over the cord and then the skin. The cremaster muscle begins, immediately to functionate and increases the strength of the inguinal region. It still retains its undisturbed relation to its anatomical origin and will undergo no alteration.

Some Disorders of the Cerebral Circulation and Their Clinical Manifestations.—RUSSELL (*Lancet*, 1909, i, 963 and 1031) says that the fundamental factor in the pathology of a fainting fit is a diminution of the volume of blood passing through the brain. Physiologically, two important factors are concerned: (1) Vasodilatation in the splanchnic area; and (2) cardiac inhibition. Probably in some cases only one of these factors is primarily concerned, in others both may be involved. It is difficult to judge as to the degree and frequency with which the heart may be affected independent of the changes in the splanchnic area. Gowers has reported three cases in which repeated syncopal attacks have passed into epilepsy. In all three the attacks were originally brought on by external influences and were typically syncopal. After a lapse of time they appeared spontaneously and with a more sudden onset, in fact, they were undoubtedly epileptic. The explanation of this change which suggests itself is that the increased suddenness of the attacks is due to increase of the rapidity with which the circulatory changes are brought about. Gowers believes that a change in the nerve elements occurs and is due to a sudden diminution of the intracranial pressure in syncope. He suggests that the resulting state of the nerve elements from repeated induction becomes spontaneous, constituting minor epilepsy. A number of cases have been reported in which it has been established beyond question that arrest of the heart preceded the epileptiform attacks. Langendorff made observations on the results of stimulation of the peripheral end of the vagus in rabbits narcotized with chloral. Electrical stimulation caused a prolonged stoppage of the heart with a complete epileptic convulsion, ten or fifteen seconds after the diastolic pause. Precisely similar convulsions are produced by compression of the thoracic aorta at a point nearer the heart than where the great vessels to the head are given off. The circulatory failure offers the most reasonable explanation for the various manifestations observed in an epileptic attack. Leonard Hill produced clonic convulsions in himself by compression of one carotid artery. Epileptic convulsions, petit mal, and infantile convulsions are probably to be explained on the basis of cerebral anemia. The phenomena of Jack-

sonian fits dependent on tumor might be due to spreading vasoconstriction.

Postoperative Pulmonary Embolism—LENORMANT (*Archiv. gén. de chir.*, 1909, iii, 221) quotes Selberg, who, upon postmortem evidence, determined that half of the deaths after aseptic laparotomies are due to pulmonary lesions. Von Lichtenberg collected statistics on 23,600 operations, of which 16,000 were laparotomies; and found that the pulmonary complications reached 2 per cent. for all operations and 5.5 per cent. for laparotomies alone. Kelting classified these cases according to the path of the pulmonary infection, into the bronchial (aspiratory pneumonias), and infection through the lymphatics (through the diaphragm from operations in the upper abdomen, especially on the stomach). Von Lichtenberg classified them into four groups: pneumonias consecuti.e to narcosis; hypostatic pneumonias; infectious pneumonias; and the embolic complications. Lenormant would add to this classification a fifth group, the pneumonias of deglutition which occur in consequence of operations on the upper digestive and respiratory tracts and in patients who vomit (intestinal occlusion). Lenormant reports briefly 4 cases of postoperative embolism, occurring in 792 different operations (a proportion of 0.5 per cent.). Three of the 4 occurred after abdominal operations. They are much less frequent after operations on other parts of the body, as the head, neck, thorax, and extremities. The danger of pulmonary embolism from laparotomy, seems to be greater the further the operative zone is from the diaphragm. Pulmonary complications are, it is true, very frequent after gastric operations, but these are pneumonias or pulmonary congestions, and emboli play in these cases, only an exceptional and insignificant role. Sometimes the emboli take their origin from the veins of the operative region, as the femoral and external iliac, especially on the left side. Lenormant believes that the latter result from an infection. As soon as a thrombus develops the danger of an embolus breaking off and being carried away in the blood stream is present. The pulmonary lesions consecutive to a pulmonary embolus vary. Massive emboli of the pulmonary trunk kill in a few minutes, by syncope. Medium and small emboli produce the classic hemorrhagic infarcts. Secondary infection of the infarct is frequent. Sometimes the infection comes from the embolus itself, sometimes from the bronchus. Odinarily the infection remains moderate and is accompanied by an embolic pneumonia. Abscess or gangrene may also result. The prognosis is extremely grave. In a series of 233 cases collected from the literature, Lenormant found 106 deaths, 45.5 per cent. The prognosis is probably less dangerous than this would indicate, since many of the milder cases are overlooked. The chief therapeutic indication is preventive. Patients with weak hearts should receive beforehand proper medical treatment. Ranzi advised preliminary injection of scopolamine-morphine, to reduce the quantity of ether necessary, while Witzel employs in such cases, ether exclusively, because it has not the depressing effect of chloroform on the heart. Strict asepsis, careful handling of the bloodvessels, especially of the veins, in the dissection of large tumors, are necessary. When the signs of pulmonary embolism develop, the usual measures to stimulate the heart and avoid asphyxia should be adopted. The operation

of Trendelenburg upon the pulmonary artery for the direct extraction of the clot can be justified only in the most grave cases in which death is imminent.

Concerning the Healing of Chronic (Tuberculous) Empyema by Means of Artificial Pneumothorax.—WENKENBACH (*Mit. a. d. Grenz. de Med. u. Chir.*, 1909, xc, 842) says that little is to be expected from the internal treatment of tuberculous empyema. The Estlander, Schede, and Delorme methods of treatment are always desperate, and when successful always leave the patient a cripple, usually an invalid. In a few cases Wenkenbach employed a method which he regards as simple and safe. In the first case several aspirations of the pus had been done, and during the last one the patient complained of oppression and pain in the chest, so that the aspiration was terminated. Through the stopcock and rubber tubing attached to the trochar, air was permitted to enter the chest, and then the stopcock was closed. The patient breathed more freely and the oppression and pain were relieved. Ten days later the aspiration of pus and the admission of air were repeated. Similar improvement followed. The treatment was repeated, at first three, and later four and six weeks apart, with complete healing finally. The patient still suffered from tuberculosis of the other lung, and gradually grew worse. In a second case, also severe, a cure was obtained. This treatment can be carried out by every general practitioner. No complicated apparatus is necessary. It is not necessary to introduce oxygen. Air is enough. The extraction of the often very voluminous exudate greatly relieves the patient. By the introduction of air the whole exudate can be removed entirely without danger. The general condition of the patient improves immediately, and the quality of the exudate is favorably changed. The lungs gradually approach the chest wall, so that the strong traction on it is avoided. The condition of the diseased side of the thorax can subsequently be improved by mechanical treatment. After a few months the patient can recover in great part or completely his ability to work.

Concerning Suture of Stab Wounds of the Lung.—STUCKEY (*Archiv f. klin. Chir.*, 1909, lxxxviii, 767) says that in recent years most surgeons have contended for radical procedures in stab wounds of the lungs. Their chief reasons for this treatment were to be found in the loss of blood, increasing pneumothorax, and progressive subcutaneous emphysema. In earlier times the fear of a general pneumothorax led surgeons to assmue a waiting position. Stuckey will follow the expectant line of treatment if thirteen hours have passed since the wound was received, unless anemia or a tense pneumothorax is present, when a radical operation will be necessary. When a stab wound is found to lead into the pleural cavity, the edges of the pleural wound should be drawn aside with sharp hooks, in order that one may obtain a view of the cavity of the pleura, and to learn whether or not there is any blood in it. If little or no blood is found, the object has been attained. The edges of the wound in the pleura and muscles should be closed with a few silk sutures. With an hermetically closed pleura, the pneumothorax will be more quickly absorbed. If there is discovered in the pleural cavity a considerable amount of blood, or there is suspected a wound of the

heart or diaphragm, a rib resection is necessary. Recent stab wounds in themselves call for operative intervention. Wounds of the lung should be closed by suture, and the suture should include the floor of the wound and not be too tightly tied. When the suture cannot be introduced and caught in the tissues, the wound should be packed with gauze and the edges of the wound sutured to the margins of the pleural opening, so that it may heal by granulation. The pleural cavity is to be completely closed by the suture, so that the resulting pneumothorax shall not give way.

A Contribution to the Surgical Treatment of Cancer of the Lip.—STEINER (*Deut. Zeit. f. klin. Chir.*, 1909, xcvii, 243) says that cancer of the lip is ten times more frequent in males than in females. Cancer of the lower lip is twelve times more frequent than of the upper lip. On the lower lip there is a predilection of the cancer to attack either the right or the left half, while in the upper lip it is generally found in the middle. Among farmers and, more particularly, smokers, cancer of the lip is especially frequent. It occurs most frequently between the ages of fifty-five and sixty years. Preceding inflammation, psoriasis, leukoplakia, and scars are exciting causes of their development. 84 per cent. of the recurrent and 71.7 per cent. of the non-recurrent cases were admitted within a year of the stated appearance of the growth; 55 per cent. of the primary cancers were admitted within the first year; in 76 per cent. the cancer had already ulcerated, and in 67 per cent. a regional gland infiltration was present; 70.7 per cent. of the cases operated on for primary cancer were free of recurrence more than three years after operation, and 69.6 per cent. after more than five years. In two-thirds of the recurrent cases death occurred in the first year; 10 per cent. of the cases operated on for recurrence remained free of recurrence more than three years. Three-fourths of the cases operated on for recurrence died in the first year.

The Treatment of Acute Inflammations with Bier's Passive Hyperemia.—LOSSEN (*Deut. Zeit. f. Chir.*, 1909, xcvii, 259) says that Bier's passive hyperemia is a valuable physical aid in the treatment of tuberculous, gonorrhœal, and acute suppurative inflammations. It is indicated, and without incision, in pure fungus, without inclination to softening, in all gonorrhœal inflammations, and in all beginning acute inflammation. It is further indicated in acute inflammations, however, only when there results a relief of inflammatory pressure from an incision or a fistula, and when for a cosmetic or functional purpose a large incision is to be avoided. It is still further indicated in those cases in which, in spite of a wide incision, the granulating wound in unhealthy and the sepsis has not diminished. Passive hyperemia is particularly effective in suppurative periproctitis, para-urethral abscesses, furuncles and carbuncles of the head and neck, suppuration of the joints and tendon sheaths, phlegmonous bursitis with fistulæ, biliary fistulæ, mastitis, softened axillary bubo, and especially in inflammations with advanced softening. It is not effective in infiltrated and fibrous inflammatory tissue (as in many streptococcic phlegmons), in glands without complete softening, lymphadenitis and lymphangitis, in many cases of bone infection, erysipelas, and diabetic phlegmons. This treatment

calls for close attention in order that the presence of retention of pus may be recognized promptly, that excessive œdema may be reduced by other physical methods, and beginning adhesions retarded.

Inguinal Hernia of the Uterus.—PARKER (*Brit. Med Jour.*, 1909, i, 947) reports the case of a woman, aged forty-seven years, on whom he did a double herniotomy. During a fortnight previous to operation, symptoms of intestinal obstruction had occurred, lasting three days. The right hernia, which alone had been troublesome, was found at operation to contain an ovary, Fallopian tube, broad ligament, and small, elongated uterus, all enclosed in a peritoneal sac. There was no means of reducing the contents, which were accordingly removed. In doing this a careful search was made for a portion or trace of the vagina, but none was found either then or after dissection of the specimen. But the finger was passed into the vagina at this stage of the operation, without obstacle and without any discovery of note. Both wounds were then closed, and they healed by first intention. Much pain and inability to pass wind, with slight but increasing distention, followed the operation. On the fifth day a median abdominal section was performed. Attached to and blocking the sigmoid flexure was found a hard lump which was taken for a small carcinoma. A loop of bowel with the lump superficial was sewn closely to the peritoneum, and its contiguous sides attached to each other in the middle of the opening. An artificial anus was then made. A careful search was made in the pelvis for the left ovary and appendages, and for the left half of the supposed uterus bicornis, but nothing whatever could be found of such parts. On attempting a vaginal examination the finger could now be passed no more than an inch or so, the vagina being tightly closed beyond this point. The symptoms of bowel obstruction disappeared, but the severe pain continued, requiring the use of morphine hypodermically. Exactly two months after the colostomy was performed a third operation was undertaken, with the view of removing the growth on the colon, which had receded into the wound. After clearing out the rectum by enemas from the fistula and rectum, the finger which passed in both directions from the fistula revealed no tumor. A clamp was applied to the spur and was gradually cut through in a little over a week, when feces were found to be passing the anus, though most passed by the fistula. A fourth operation was done to close the fistula. This did not succeed, but later the fistula gradually closed and the patient became perfectly well.

Tetanus Occurring after Surgical Operations.—RICHARDSON (*Brit. Med. Jour.*, 1909, i, 948) reports two cases in which the symptoms of tetanus developed after operation, one for gallstones, the other for a strangulated, inguinal, omental hernia. Both patients died. Richardson collected notes of 21 cases in which tetanus followed operation. Twenty of the cases have occurred within the past three and one-half years, and one as long ago as 1884. Hamilton has pointed out that there is a group of diseases among sheep, the symptoms of which are closely allied to tetanus and the bacillus of which cannot be distinguished from that of tetanus. These diseases are endemic in certain parts of the British Isles. The 21 cases have occurred only in those districts in

which the tetanic group of sheep diseases is endemic. More than 90 per cent. of the cases of postoperative tetanus followed operations in which the peritoneal cavity had been opened. Richardson suggests that the disease which we call postoperative tetanus is not tetanus at all, but one of the sheep diseases; that it is not introduced by the catgut; that the patient is at the time of the operation the host of the bacillus; and that we must look upon these as cases of idiopathic tetanus, accepting Hamilton's suggestion that idiopathic tetanus is not true tetanus as we understand the term. The most important point is to determine whether the infection, whatever it may be, is conveyed by the catgut. Richardson hopes that the catgut may be acquitted.

Concerning Excrescences of Fatty Synovial Fringes in the Knee-joint.—RAMMSTEDT (*Archiv f. klin. Chir.*, 1909, lxxxix, 173) says that no joint in the body is subject to so many injurious influences as the knee. While much attention has been given in the literature, recently, to many of these conditions, relatively little has been given to the inflammatory overgrowth of the fatty masses and fringes in the joint. Hoffa, who first called attention to them, on opening a joint for a supposed injury to the semilunar cartilages, found this condition, and upon excising the fringes a cure followed. They spring from the ligamenta alaria and mucosa, increase in size from inflammatory hyperplasia, and because of their increased size become caught between the ends of the bone, producing severe symptoms. The causative synovitis may be due to trauma or disease. The catching of the fringes between the ends of the bones may be confused with a dislocation of a semilunar cartilage, a free joint body, or a tearing of a crucial ligament. In the latter group of conditions the severe symptoms are followed by synovitis and effusion into the joint. In the case of catching of the fatty fringes, almost always a chronic swelling of the joint, and especially of the fatty masses at the sides of the ligamentum patellæ, precedes the occurrence of the severe symptoms. One should bear in mind that isolated lipomas and sarcomas have been reported. The lipomas may be of various sizes, from that of a hazel-nut to that of a walnut, and may give symptoms simulating those produced by the catching of the fringes and may also be preceded by trauma. The treatment of cases in which the fringes are caught may be conservative if they give only moderate disturbance. In most cases, improvement and a gradual return to the normal follows the use of massage, heat in the form of sand baths or hot air, elastic compression by bandages, and guarded use of the joint with apparatus. Patience is especially necessary. Operation is justified in the more severe cases with limitation of movement and severe pain associated with locking of the joint. The joint should be opened freely by a curved incision at the outer or inner side over the prominence. The hypertrophic masses are then seized with forceps and excised with suitable scissors. The hemorrhage is slight and can usually be stopped by a gauze pad, which may be left in position until the capsule wound is about to be closed. Drainage is not necessary. If an effusion of bloody serum should form, this may be removed by puncture on the first change of the dressing. In from twelve to fourteen days after the healing of the wound, massage, hot air, movements of the joint, and compression bandages should be employed.

THERAPEUTICS.

UNDER THE CHARGE OF

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The Therapy of Diabetes Mellitus.—FALTA (*Archiv. Int. Med.*, 1909, ii, 159) calls attention to the fact that human diabetes mellitus is a highly complicated disease often of widely different etiology. He thinks that the diabetic disturbance of metabolism may be broadly defined as a lack of equilibrium between carbohydrate mobilization and carbohydrate metabolism, arising from deficiency of the pancreas or from overactivity of the chromaffin system, or from both causes together. Accordingly, a causal therapy is out of the question. Attempts have been made to increase the efficiency of carbohydrate metabolism by increasing or supplying the internal secretion of the pancreas, but as yet Falta says that the results are unsatisfactory and impracticable. A diminution of the excessive carbohydrate mobilization might be brought about by checking the activity of the nervous system. Falta thinks that some of the favorable results obtained by the use of sedatives may be thus explained. The theoretical principle of dietetic therapy is to diminish the demands upon the diseased organ or organs and give them thereby the opportunity of recovering.

Falta first considers a small group of cases which manifest a marked disease of the pancreas. In these cases protein and fat are imperfectly absorbed, as evidenced by their presence in increased amounts in the stools, and in addition carbohydrates are excreted, as evidenced by the glycosuria. It is essential, Falta says, to replace the pancreatic secretion in the treatment of these cases. For this purpose the most useful preparation is the pancreatin of the Rhenania factory in doses of 10 grams daily. Alkalies must be used in conjunction with the pancreatin. Von Noorden prefers the use of calcium carbonate, which is less readily absorbed from the stomach than sodium bicarbonate, for this purpose. Emulsified fat (as milk or the fat of egg yolk) is much better utilized by these patients than other fat preparations.

Falta points out that the measures by which glycosuria may be diminished may have to be considerably modified in some of the acute and chronic infectious processes, which frequently complicate diabetes. Thus, for instance, a strict diabetic regimen may be harmful in a complicating pulmonary tuberculosis. However, in the milder forms of pulmonary tuberculosis complicating diabetes, Falta has noted an improvement with the disappearance of glycosuria after appropriate dietetic treatment. He maintains that each individual case has its own peculiar characteristics, and therefore the glycosuria must be combated only after a careful preliminary estimate of the character and intensity of the disease. He makes use of a test diet over a period of three days. This test diet consists of 250 grams of meat, 150 grams of butter, 4 eggs, 300 grams of vegetables with a low carbohydrate value, tea, coffee, bouillon, about

4 deciliters of light white wine, and 75 grams of white bread divided into three equal portions. This diet contains, approximately, 16 grams of nitrogen, 50 grams of carbohydrates, and about 2400 calories. On this diet a certain number of cases will preserve a so-called positive carbohydrate balance; that is, they will excrete a less amount of sugar than corresponds to their carbohydrate intake. Falta gives formulas which help to determine the source of the glycosuria in those cases in which there is a so-called negative carbohydrate balance. The test diet also allows a rough estimation of the ketonuria. The age, occupation, surroundings, duration of the diabetes, and possible complications should also be considered in order to arrive at a conclusion concerning the severity of the disease. In the mild cases, the elimination of bread from the test diet will usually make the patient sugar free. In severer cases, in which the withdrawal of the carbohydrates does not suffice, we decrease the nitrogen content of the food to about 8 grams and increase the amount of butter to about 200 grams. If this also proves insufficient, it is advisable to introduce one or two days of vegetable diet; or, according to Naunyn, one day of fasting; or, according to von Noorden, an "oatmeal cure." Falta emphasizes the necessity of a close watch of the ketonuria, especially in the severer cases. It is easier to prevent the occurrence of a ketonuria than to suppress an existing ketonuria, and therefore Falta rightly says that this prevention is the fundamental point in the treatment. This is accomplished by the administration of alkalies during the period of withdrawal of the carbodydrates. The reaction of the urine, according to Falta, affords an excellent sign of the degree of acidosis. If the urine becomes alkaline, the acids surely have been neutralized. If a marked ketonuria is present, it is better to saturate the body with alkalies as quickly as possible, and when the urine has become alkaline to decrease the dose gradually, but always to keep the reaction of the urine slightly alkaline. At this stage usually a part of the sodium bicarbonate is replaced by sodium citrate. If the administration of alkalies is not sufficient to neutralize a high degree of acidosis, it is necessary to decrease the formation of the ketones. Large quantities of alcohol decrease slightly the formation of ketones. However, the carbohydrates are our main reliance for the reduction of the formation of ketone bodies. Falta says that it is best to give a low diet containing from 8 to 10 grams of nitrogen and not more than 150 grams of fat, with the addition of 100 or 150 grams of carbohydrates in the form of fruit, milk, oatmeal, etc. This naturally produces an increase of the sugar content of the blood, which should then be lowered by the interposition of two or three "vegetable days," with 50 grams of carbohydrates.

For the treatment of diabetic coma, Falta advises a diet consisting almost exclusively of carbohydrates, with the addition of 50 to 100 grams of levulose. Enormous doses of alkalies are necessary, and Falta recommends the intravenous method as the best method of administering them. He advises one liter of a 4 per cent. soda solution for this purpose. In the treatment of those patients who have become sugar free by the withdrawal of carbohydrates, Falta follows Naunyn's suggestion and keeps them two weeks on the diet by which they have become sugar free. Then bread is gradually added to the limit of tolerance. Finally, half the amount tolerated is given to the patient and variety is introduced

into the diet by means of fruit, cream, vegetables, and various kinds of bread. In those cases in which it has been necessary to reduce the amount of proteins, the nitrogen in the diet should first be increased to 12 or 14 grams. When the patient has been sugar free for three or four weeks, carbohydrates should be added. The kind of carbohydrate tolerated by the individual case may differ widely. Levulose and lactose are tolerated by some diabetics, but increase the glycosuria in others.

Falta says that especial care is necessary for those cases who do not become sugar free by the withdrawal of carbohydrates and the reduction of protein. Such cases are at times rendered sugar free by the introduction of "hunger days" or "oatmeal cures." Falta believes that the "milk cure" only diminishes the glycosuria in diabetic patients, who were formerly overnourished and are insufficiently nourished on a strict milk diet. He discusses the "potato cure" as of no value. He believes that the "oatmeal cure" has both theoretical and practical value. He describes the present method of giving the "oatmeal cure." After several days of strict diet come two vegetable days, then three oatmeal days, and finally two vegetable days. After the vegetable days, strict diet with diminished protein is given. On each oatmeal day the patient receives 250 to 300 grams of oatmeal, prepared with an equal quantity of butter and divided into five portions. Black coffee, wine, or a little brandy may be added to the diet. If there is any diarrhœa, Falta advises the use of a few drops of tincture of opium. In all but a few cases the ketonuria is diminished, and the most important indication for the "oatmeal cure," therefore, is the combating of ketonuria. In addition the patient has assimilated a considerable amount of carbohydrate without a corresponding increase in the hyperglycemia.

Falta adds some general points in the therapy of diabetics. He says that the treatment of patients with ketonuria is only possible outside of hospitals if they are very intelligent. A course at one of the many spas is often of great assistance in the treatment. He also includes carefully regulated exercise as a very important element in the treatment.

The Treatment of Contraction in Hemiplegia.—Von Criegern (*Fortschrit. der Med.*, 1909, i, 1) believes that many of the phenomena of contractures are due to congestion in the parts affected. The cramps in the muscles which are caused by unaccustomed exercise are, in Criegern's opinion, analogous to some hemiplegic contractures. The sensation of stiffness in the arms which follows rowing is due to congestion, and is relieved if the exercise is persisted in, or if the blood is allowed to pass out of the limbs by raising the arms above the head. In applying this principle to the conditions found in hemiplegia a month or longer after the onset, several methods may be employed. The contracture subsides after the application of an Esmarch bandage, and then the muscles may be exercised. Sometimes it is found best to defer exercise until after the removal of the bandage, which should always be done with the limb raised. The arm should be worn in a sling or held in an elevated position in order to avoid congestion. Criegern has noted that the paralysis often is not so marked as it had been supposed to be before the congestion had been reduced, and relates in detail the case of a man who had partially recovered from a hemiplegia two years before. His right arm was quite

powerless, and a severe degree of contracture of the hand had resulted. After three months of treatment by induced anemia this patient was able to use his hand in eating and dressing, and improvement was continuing at the time of this report. This method is not so easy to apply to the leg as to the arm on account of the difficulty in keeping the leg raised, and here an elastic stocking is advisable. The treatment is the reverse of the hyperemic method and has yielded excellent results in Criegern's hands.

Phosphorus in the Treatment of Rickets.—The action of phosphorus in rickets has not been satisfactorily studied with reference to the calcium metabolism, and for this reason SCHABAD (*Zeitschr. f. klin. Med.*, 1909, lxvii, 454) has examined the calcium metabolism of healthy and of rachitic children before, during, and after the administration of phosphorus. His results are detailed at great length, and lead to the following conclusions: (1) In therapeutic doses phosphorus produces no change in the calcium metabolism of healthy children, but it leads to a well marked retention of calcium in rachitis. (2) The retention is to be attributed to the increased absoption and the diminished excretion of calcium in the urine and feces. (3) The retention of calcium may be noted soon after the exhibition of phosphorus (three to five days); after the withdrawal of the drug this retention persists about two months (following its previous administration for two and one half months). (4) Phosphorus exerts a specific action on rachitic bones and raises their calcium content, so that the latter approaches the normal.

The Treatment of Chronic Asthma and Emphysema.—BOELLKE (*Med. Klin.*, 1909, viii, 283) has used pyrenol in the treatment of 39 cases of asthma and emphysema. He gives it in doses of from 3 to 4 grains per day. Pyrenol is a combination of Siam benzoic acid and thymol with synthetic benzoic acid and oxybenzoic acid. The Siam benzoic acid gives it expectorant properties, which are enhanced by the thymol. In addition, the thymol has anesthetic properties. The distressing dyspnœa is relieved in three or four days, the cough loses its hard and paroxysmal character, and expectoration becomes looser and easier, generally on the second day. At the same time the disturbances of the circulation disappear. A number of the patients experienced a sense of well being to which they had long been strangers. Coincidently the signs of bronchitis cleared up, in many cases entirely so. A relapse occurred in one case only. Boellke did not observe any untoward effects upon the heart, kidney, or gastro-intestinal tract in the use of pyrenol. He observed no cumulative action and no diminution of the effect of the drug after long-continued use. Heart, kidney, and bronchial complications are no contra-indications for the use of pyrenol. Boellke states that patients who had formerly been treated with atropin or potassium iodide thought that pyrenol gave them the greatest relief.

PEDIATRICS.

UNDER THE CHARGE OF
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An Epidemic of Cerebrospinal Meningitis in Paris; Efficacy of Antimeningitic Serum.—In opposition to the usual belief that there is very little cerebrospinal meningitis in Paris, NETTER (*Bull. de l'acad. de méd. de Paris*, 1909, lxi, 300) reports a small epidemic. He, himself, has seen and treated 22 cases within the short space of three months, most of them in children and infants. Many of the patients lived within a small circle; and 6 of the children attended one school. Several of the children died within a few days and the diagnosis could only be made postmortem through lumbar puncture, the serum being turbid and containing the diplococcus of Weichselbaum. The symptoms varied greatly in the different cases, but the lumbar puncture made the diagnosis a certainty in each instance. Macroscopically, the fluid in all was turbid; microscopically, lymphocytosis existed and the Weichselbaum organism was found to be present. Netter emphasizes the importance of isolation until the nasal and pharyngeal mucus is free of organisms known to bear an etiological relation to the disease. He appreciates the difficulty, but feels that this is one of the most important problems in combating the disease. Fifteen of his patients were treated with antimeningitic serum, and but 3 of these died; these deaths occurred, respectively, in one patient with old otitis media and phlebitis of the ophthalmic vein, in another with bronchopneumonia and enteritis, and in a third who was not treated until moribund. The technique of the treatment, the changes in the symptoms, and the modifications in the cerebrospinal fluid are described minutely. The latter changes form a perfect control to the employment of the serum. He injects the serum into the spinal canal, using doses varying from 20 to 30 c.c. in children, and repeating the injections daily for three to four days. He is very enthusiastic about the results achieved.

Congenital Imperforation of the Œsophagus.—P. GIBERT and J. LEMEE (*Bull. et mém. de la soc. anat. de Paris*, 1909, lxxxiv, 94) report a case of congenital imperforation of the œsophagus in a child aged seven days. Within a few moments after nursing the child regurgitated all the milk spontaneously. This regurgitation was always accompanied by marked cyanosis. Having seen 5 cases of congenital imperforation of the œsophagus within fifteen mouths, this condition was at once considered, and local examination revealed this to be the true state of affairs. The soft catheter could not be pushed beyond 12 cm. from the buccal orifice. A tracheo-œsophageal fistula was suspected because of the marked cyanosis after nursing and at other periods, when saliva would be vomited up. This condition was verified at the autopsy, the upper third of the œsophagus being represented by a pharyngeo-œsophageal cul-de-sac, the lower two-thirds by a canal

extending from the stomach to the trachea, opening into it at its posterior surface 3 mm. above its bifurcation and there separated from it by a valve.

Grave Intestinal Hemorrhage in the Newborn.—GUERIN-VALMALE (*Bull. de la soc. d'obst. de Paris*, 1909, xii, 97) reports the following case: A little girl, born without difficulty of healthy parents, was exposed to considerable cold air shortly after her birth. She sneezed and cried a great deal from her birth on. She vomited after every nursing, but took the breast well during the first forty-eight hours; by that time she was so weak that she could hardly cry or nurse. On the third day a hemorrhagic eruption appeared in different parts of her body, especially, however, over the buttocks. The child became very anemic, and was constantly in partial stupor. The stools, which, until now, consisted of meconium, contained considerable blood, and several times during the next few days seemed to be composed of pure blood. Chloride of calcium was given with the mother's milk from a spoon, and adrenalin was ordered by lavage. This condition continued for a week, some blood also being discharged by the vagina. Recovery finally, however, was complete, and a month later the child bore no further traces of the hemorrhages. Discussing the cause, Guerin-Valmale excludes prenatal infection, as the mother was perfectly well during the entire pregnancy; postnatal infection, as no signs of any such existed, even the umbilical cord falling off without any trouble; syphilis, there being no history of any. He considers the case to be one of hereditary tendency to hemophilia, the maternal side being remarkably nervous, the paternal side containing several individuals with a tendency to epistaxis and other bleeding. The chilling immediately after birth is considered the exciting cause.

The Antitoxic Properties of Gastric Juice and its Importance in Infant Feeding and Immunity.—Several years ago A. SCHULTZ published the results of certain researches, which showed him that the gastric juice of the newborn and nursing infants destroys the diphtheria toxin; this property he found to pertain to all stomachs functionating normally and not to present any individual variations, which would depend on age, or the mode and state of nutrition of the child. This was found to be due to an organic substance, some importance also being attributed to the degree of acidity of the solution. New studies along the same line performed by him (*Zeit. f. Hyg.*, 1909, lxi, 115) produced the following results and conclusions: (1) The diphtheria toxin is destroyed by a solution of hydrochloric acid, the amount of free acid of which corresponds to the gastric juice of a nursing infant. (2) The action in vitro appears after a certain reaction time (more than fifteen minutes). (3) In vivo the free hydrochloric acid continues to act subcutaneously on the poison, if the inoculation is performed immediately after they are mixed. (4) Hydrochloric acid fixed by egg albumin is without influence on the diphtheria poison, but when fixed with peptone it destroys the toxin. (5) Hydrochloric acid loses its activity when added to cow's milk and cooked human milk, but when combined with ordinary mother's milk the diphtheria toxin is destroyed by the mixture. (6) Combined hydrochloric acid is weaker in its action on diphtheria poison than is

free hydrochloric acid. (7) The reaction appeared as quickly in most of the experiments, whether combined or free hydrochloric acid was employed, as long as equal quantities of the solution were used. If the amount of free hydrochloric acid was smaller, the appearance of the reaction was correspondingly slower. (8) The amount of the antitoxic power of both free and combined acids equals their antiseptic properties. (9) The concentration of the pepsin solution employed is forty times stronger than the pepsin strength of the gastric juice of the nursling; it destroys the diphtheria toxin as quickly as does the hydrochloric acid solution, and no free hydrochloric acid need be present in the pepsin solution. (10) The destruction is complete after one minute, the reaction beginning immediately. (11) The acid pepsin solution quickens the results reached with combined hydrochloric acid; it increases the digesting power so much that the destroying power of the pepsin solution containing combined hydrochloric acid is almost equal to that of free hydrochloric acid. (12) The alkaline pepsin solution is without power. (13) Rennet does not act on the diphtheria poison; lactic acid destroys it. Hydrochloric acid combined with mother's milk possesses an antiseptic power equal to that of free hydrochloric acid. In the case of breast-fed children the disinfection of the stomach occurs therefore not only toward the end of the digestive period, but also to some degree during it. This is of especial importance in the cases of children, who, while being artificially fed, are seized with intoxications and infections associated with gastro-intestinal symptoms, and explains why such children recover much more quickly from such diseases when their nourishment is changed to mother's milk.

Ovarian Cysts in Childhood.—CHENEY (*Pediatrics*, 1909, xxi, No. 3) reports a case of ovarian cyst in a girl, aged sixteen years, who had been previously healthy. Menstruation had been regular and normal for two years. She had noticed a growth in the abdomen for about two months, had no fever and few symptoms except discomfort and occasional pain. A large tumor was found occupying the entire left half of the abdomen and extending down into the pelvis, its upper border not connected with the spleen. The outline was regular and felt solid or semisolid. It partly filled the pelvis and had pushed a normal uterus downward and backward. Examination of the blood yielded negative results. On operation a papillary cystadenoma of the left ovary, weighing nine and one-half pounds, was removed. Cheney states that ovarian tumors are not uncommon in childhood, being more frequent as puberty approaches. They are cystic or solid, and include sarcoma, carcinoma, and dermoid cyst. Of all classes multilocular cysts, or cystadenoma, are the most common. He refers to Howard Kelly's collection of 126 cases of ovarian tumors in children. Of this number number, 55 were cysts, 47 dermoids, and 24 solid tumors. The youngest patient reported was an infant, aged four months, the next were three years and four years respectively. In diagnosis ovarian cysts must be differentiated from dermoids and sarcomas of the ovary; from peritonitis with encapsulated effusion; from malignant and cystic disease of the kidney; and from retroperitoneal affections.

OBSTETRICS.

UNDER THE CHARGE OF
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Convulsions in the Newborn.—Esch (*Archiv f. Gynäk.*, 1909, lxxxviii, Heft 1) reviews the literature of this subject, in which the mortality of convulsions in the newborn varies from 25 to 100 per cent. The frequency of this complication is reported as from 0.13 per cent. to 2.69 per cent. The cause of the convulsions is most frequently umbilical infection, then œdema and asphyxia, then syphilis, and hereditary eclampsia. Among the illustrative cases reported is one by Stöckel, of a female child delivered spontaneously after normal labor. For the first day after birth the child was restless, cried frequently, and showed in the face great pallor. In the morning of the second day it vomited, and the greater fontanelle was protuberant. Spasms of the limbs, fingers, and toes, with stiffness of the back, developed, and pressure upon the internal surface of the arm produced spasmodic closure of the fist. On the evening of this day the child suddenly became deeply cyanosed, and tonic convulsions developed throughout the muscular system. On the third day the convulsions ceased, but there was increased muscular irritability in the arms and legs and the muscles of the back. On the fourth day the symptoms were less pronounced, and the child ultimately recovered. No signs or history of syphilis could be detected. The case was diagnosticated as cerebral irritation occasioned by bleeding above the tentorium without special localization of the lesion. As the hemorrhage gradually ceased, and was not profuse, the child recovered. Auto-intoxication of intestinal origin, may also produce convulsions, as illustrated by the following case: The birth of the child was spontaneous, and the mother apparently healthy. The child cried and vomited excessively during the second day of its life. There was increased muscular and nervous tension of the extremities and back. Meconium was discharged freely. On the next day the bowel movement was yellowish in color, vomiting continued, and the hypertonic condition of the muscles was more pronounced. The abdomen became swollen, and on the day following fluid could be diagnosticated in the abdominal cavity. Death occurred shortly after. There were no clonic convulsions. Upon autopsy a thick, yellowish brown membrane was found lining the abdomen, composed of fibrin and white blood cells. The abdominal fluid contained intestinal bacteria, leukocytes, and erythrocytes. The intestines were matted together. On separating them a perforation of the bowel was found at the jejunum and the borders of the perforation showed infiltration with small cells. The contents of the bowel escaping into the peritoneal sac had caused death. There was also hyperemia in the lungs and membranes of the brain, with petechial hemorrhage in the pleura, and hemorrhage in the uterus, membranes, and stomach. The cause of the intestinal perforation could not be clearly distinguished. Esch calls also attention to pathological conditions in the medulla causing convulsions in the new-

born. He cites the case of a child nursing poorly on the third day, and seeming oppressed or stupid. On the fourth day cyanosis developed with regurgitation of food. Spasms of the muscles of the extremities and back appeared, varied by clonic spasm. The temperature was much below normal, and the child seemed collapsed. The bowels moved freely. On the day following there was a free discharge of mucus from the mouth and nose. The breathing became labored and the child died. At autopsy no jaundice was found, the heart was normal, the lungs contained air, and there was no pneumonia. The spleen was enlarged and dark red; the suprarenals were large but without excessive fat, and with no hemorrhage. The kidneys were engorged with blood; the liver was filled with blood, and large and yellowish brown in color; the stomach and intestines were normal; there was no tumor upon the cranium or scalp; there was no rupture of the superior longitudinal sinuses; and in the subdural spaces there was some thickened blood. The tentorium was distended and tense. The cerebrum showed no hemorrhage and its configuration was normal. In the cerebellum there was pronounced hemorrhage, sufficient to alter the contour of this portion of the brain. The fourth ventricle was greatly compressed, but contained no blood. There was also pressure upon the medulla and pons. The meninges of the cord contained fluid blood, but the cord itself was normal. He also reports the case of an infant born by version and extraction because of prolapse of the cord and transverse presentation in a flat rachitic pelvis. The child was cyanotic after birth. After efforts at resuscitation the child breathed spontaneously, but died soon after. Section showed the occipital bone pressed under the parietals, and hemorrhage in the region of the cerebellum. Esch also calls attention to the fact that in the case of a child dying a few days after birth, disturbances of nutrition, with the development of pneumonia, may produce convulsions similar to those observed in cerebellar lesions in the newborn.

Axillary Milk Glands Developing during Pregnancy.—Seitz (*Archiv f. Gynäk.*, 1909, lxxxviii, Heft 1) contributes a paper upon this subject, reviewing the literature, and giving illustrations of cases with microscopic drawings of specimens removed. He concludes from his studies that the sweat glands of the axillary region increase in size and function during pregnancy, as do the mammary glands. Under conditions not clearly recognized, these axillary glands become greatly enlarged during pregnancy and the puerperal period. In addition to the glands normally found in this region, others may develop to an extraordinary degree. Some take on the shape and function of milk glands and show the characteristic secretion. Microscopic examination shows the structure of these to be practically identical to those of the enlarged sweat follicles. As these glands are without excretory ducts, they become distended, and are largest in size from the fifth to the seventh day of the puerperal period. They usually subside by the fourteenth day. These glands have nothing to do with so-called accessory mammary glands, or with the auxiliary follicles sometimes found about the nipples. They are more often seen in patients who have highly developed mammary glands. When these tumors are examined microscopically, they might readily be mistaken for adenoma. The fact that the swelling occurs during pregnancy and the puerperal state, should

make clear the diagnosis. A somewhat similar swelling is sometimes observed at menstruation.

The Practical Value of Antistreptococcic Serum.—HEYNEMANN and BARTH (*Archiv f. Gynäk.*, 1909, lxxxviii, Heft 1) have investigated by bacteriological and clinical studies several of the antistreptococcic sera now employed. They find that those supplied by Höchter, Merck, and Schering give results which are more or less discernible. In none of the cases observed did the serum equal in potency the serum of a normal puerperal patient. In fresh serum obtained by these different substances the potency was never so great as that of normal serum from a normal puerperal patient. With a diluted antiserum 1 to 1000, a more pronounced phagocytosis was obtained than with a diluted normal serum. This result was not altered when fresh normal human or horse serum was added as a complement, or by the use of leukocytes obtained from the horse. The potency of antistreptococcic serum does not depend upon its containing substances causing phagocytosis. With serum of the highest potency in doses of 100 c.c. no results were obtained in puerperal streptococcic infection. Experiments upon animals should be conducted with the hope of obtaining a more efficient serum of high potency, which can be used in the streptococcic infection of parturient women.

Indications and Prognosis of Operations for Gallstones Performed during Pregnancy.—ROITH (*Monatssch. f. Geb. u. Gyn.*, 1909, Band xxix, Heft 4) reviews the literature of the subject, finding but 9 reported cases; 8 of these are reported as recovered; in but one did the uterus empty itself fourteen days after the operation, and this patient died; one patient aborted after operation, but recovered. Pus was present in the gall-bladder in 5 out of the 9 cases. All of them were before full term with one exception, and this patient's case terminated fatally, labor occurring fourteen days after the operation; 4 of the cases were treated by cholecystectomy with drainage of the hepatic duct; 4 by cholecystotomy; and one by sewing the edges of the gall-bladder to the edges of the abdominal incision. These cases indicate that pregnancy is not a contra-indication against the operations upon the gall-bladder and bile ducts. The prognosis is not made especially grave by the occurrence of pregnancy. The probability of the interruption of pregnancy depends upon the period of gestation, the intensity of the jaundice and the infection, and the extent and time occupied in the operation. During the first half of pregnancy the danger of interruption is very little. Toward the end of pregnancy the danger of interruption increases, and incisions obliquely along the borders of the ribs, and cystotomy, are the method of choice. By this method the operation is made as brief as possible, and the uterus is disturbed as little as possible. In severe cases at the end of gestation the patient should be delivered before the operation upon the gall-bladder is undertaken. Vaginal Cesarean section seems indicated in these cases, because the incisions for delivery are removed from the area of infection, and infection is less likely to occur. When labor pains develop after operation the uterus should be emptied as soon as possible, because uterine contractions tend to spread infectious matter from the hepatic wound into the peritoneum. Anesthesia in these cases requires especial attention.

GYNECOLOGY.

UNDER THE CHARGE OF

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Non-surgical Treatment of Uterine Displacements.—H. J. BOLDT (*Jour. Amer. Med. Assoc.*, 1908, li, 903) makes a plea for treatment, other than surgical operations, for displacements of the uterus. Boldt believes anterior displacement of that organ requires no treatment but that by pessaries; acquired retrodisplacements free of adhesions are successfully treated by properly applied pessaries, preferably of the Smith or Thomas variety. Boldt, after fully describing methods of replacing the uterus so displaced, states that pessaries should never be applied when the uterus is not in proper position.

Injuries to the Bladder during Hernia Operations.—R. E. SKEEL (*Amer. Jour. Obst.*, 1908, lviii, 964) states that injuries to the bladder taking place during operation for the ordinary forms of hernia are of two distinct classes, as pointed out by Bruner in 1898. The first and probably the least common form occurs from the presence within the sac of the bladder or a diverticulum therefrom; or in the paraperitoneal form the bladder escapes along the side of the hernial sac and is injured when the latter is incised or ligated; or otherwise damaged when the neck of the sac is dissected from subjacent tissues. The other and commonest form is probably due to traction upon the sac in an effort to ligate it as high up as possible, with the result that the peritoneum passing from the bladder to the pelvic wall is dragged into the incision, carrying the bladder with it, where it is either ligated, incised, or torn. Skeel has collected 325 cases, of which 225 were in males, 80 in females, and in 20 the sex is not given. Of the males, 216 were inguinal, 4 femoral, 1 of both varieties, and in 4 the variety is not definitely stated. In the female 21 were inguinal, 50 femoral, and in the remainder the variety is not given. In Bruner's statistics 59.5 per cent. of the cases in which the bladder was recognized it was injured, while in the cases collected by Skeel since 1896 this rate fell to 27.6 per cent. The mortality rate was about 24 per cent. For the purpose of positively identifying the bladder when opened by accident Skeel advocates the routine use of methylene blue for a day or so prior to the herniotomy.

The Menopause.—D. H. CRAIG (*Jour. Amer. Med. Assoc.*, 1908, li, 1507) believes there are three normal types of the menopause, sometimes seen more or less in combination with one another, and departures from these types are easily recognized. The symptomatology alone will very often point to the organ or region at fault, but such deduction should always be given physical confirmation. Lesions at this time are as deserving of and amenable to treatment as at any other time, and neglect of such treatment engenders inestimable, unnecessary suffering, and is one of the greatest factors in causing so many malignant

uterine growths to attain an inoperable state of advancement. Failure properly to diagnosticate and treat such cases will inevitably bring opprobrium on the profession as a whole.

Experimental Contributions on the Operative Treatment of Acute Puerperal Peritonitis.—ZANGEMEISTER (*Ztschr. f. Geb. u. Gyn.*, 1908, v, lxii, 510) reports the results of several series of experiments with streptococcic infection of mice. He injected a diluted quantity of streptococcus culture into the tails of these animals and then amputated them. He found that the removal of the infected area delayed death. Antistreptococcic serum given alone prolonged life also. If, however, amputation and serumtherapy were combined, the effect was augmented to such a degree that none of the animals died, which showed conclusively that the highly curative properties of an effective antistreptococcic serum may be considerably increased by the simultaneous removal of the site of primary infection. The conditions in puerperal peritonitis are very unfavorable, as usually more than half of the period of time between infection and death has passed before symptoms leading to operation appear, nor can the site of primary infection be so readily removed as in animal experiments, and finally, the operation needed is such as greatly to tax the resistance of the organism. In view of these facts, he considers it very doubtful whether the operative removal of the primary seat of infection without simultaneous serumtherapy in acute puerperal streptococcic peritonitis could be successful. The prognosis is much more favorable if the operation is combined with serumtherapy. In such cases the removal of the uterus and adnexa by the abdominal route is advised.

Renal Decapsulation in Eclampsia.—KEHRER (*Zeit. f. Gyn., u. Urol.*, 1908, i, 111) collected and analyzed all cases of eclampsia treated by renal decapsulation of Edebohls, and arrives at the following conclusions: (1) Decapsulation is misapplied when employed in eclampsia during pregnancy. In such cases the detoxinizing therapeutic measures and accouchement forcé are indicated. (2) According to our present knowledge decapsulation is indicated in those severe cases of puerperal eclampsia in which the kidneys are involved to a considerable extent, and it should be recommended in the cases in which, in spite of delivery, venesection, and application of all other measures known to stimulate the excretory organs, the attacks grow worse and the general condition becomes aggravated. In such cases only a few hours should be allowed to elapse before decapsulation is performed. (3) Edebohls' operation excites increased urinary and urea excretion and a simultaneous increase of excretion of the eclamptic toxin in the circulating blood. (4) The success of the decapsulation rests in the increased diuresis which is a physiological and not an anatomical result. The anatomical basis for operation on which Edebohls, O. Franck, and others rely, namely, development of vascular anastomoses between the renal surface and the adipose capsule, does not exist. (5) The improvement in the albuminuria, hematuria, and cylindruria occurs synchronously with increased diuresis, or soon follows. The disappearance of these signs depends directly on the degenerated conditions of the renal parenchyma at the time of operation. This explains why chronic and suddenly increased

inflammatory processes are little or not at all affected. (6) The precise indication for operation and the further study of the influence of the decapsulation on the activity of the kidney and the entire organism depend on most careful functional tests of the kidneys. Microscopic examination of the excised pieces of kidney and comparison with the functional tests before and after operation may also serve to fix accurately the time when decapsulation should be done. It may be possible to ascertain in this way whether in all cases in which indication for decapsulation is recognized bilateral operation is necessary or whether unilateral decapsulation suffices. The effect of massage of the kidney should also be studied experimentally. (7) In Edebohls' renal decapsulation of the kidneys we seem to possess a remedy in severe cases of eclampsia, and there is hope that a portion of the 20 per cent. of cases of eclampsia which do not improve after the uterus is emptied, or those which occur thereafter, may be cured by renal decapsulation at the proper time. The cases of degenerative changes in other organs, particularly of the liver and the heart, cases of pulmonary œdema, and of hemorrhages in internal organs remain hopeless. The future will show whether renal decapsulation is justifiable or whether later renal function is impaired by enclosure of the kidneys in inelastic connective tissue bands.

Inflammatory Proliferation of the Mucous Membrane with Epithelial Hyperplasia in the Fallopian Tube.—M. NEU (*Zeit. f. Geb. u Gyn.*, 1909, lxii, 489) reports the case of a woman, aged fifty-one years, with pulmonary tuberculosis, who developed an irreducible prolapse of the adnexa into the vagina after vaginal total extirpation of the myomatous uterus. At the time of the operation the adnexa appeared to be quite normal. An unusually abundant suppuration followed the operation. The prolapsed adnexa became involved in the inflammatory process, particularly the more deeply situated adnexa on the right side. As a result a suppurative inflammation of the tube and ovary developed which passed into a chronic inflammatory condition. The secretion was finally disposed of by removal of the prolapsed adnexa in the vagina about a year after the operation. The portion of removed tube was cut into a series of 245 sections and examined microscopically. It showed all the characteristic signs of a purulent and hemorrhagic salpingitis and proliferations of adenoma-like character of the partly stratified tubal epithelium.

Malignant Tumor of the Ovary Complicated by Twisted Pedicle.—GUIBE (*Ann. de gyn. et d'obst.*, 1909, xxxvi, 110) reported a case of sarcoma of the ovary the pedicle of which organ was many times twisted. The patient, a healthy peasant, aged sixty years, was admitted to the hospital for intestinal obstruction, that had supervened after a severe attack of coughing that immediately gave rise to severe pain in the hypogastrium four days before. The blackened friable tumor mass of the size of two fists was removed. Pulmonary complications began ten days after operation and ended fatally six days later. When malignancy of a growth of an ovary is suspected and its removal decided upon, both appendages and the body of the uterus should be removed, is the advice offered by Guibe, who comments also on the comparative rarity of twisting of the pedicle of solid ovarian tumors as compared to cystic ones.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES.

UNDER THE CHARGE OF
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Asymmetry of the Hard Palate.—Mosher (*Laryngoscope,* April, 1909) contributes an instructive and well-illustrated paper on "The Form of the Hard Palate," showing the effect of asymmetry upon the teeth, rhinopharynx, nasal fossæ, and contiguous structures. He deems asymmetry of the two sides of the hard palate due to unequal descent of the antrum or to unequal growth of the superior maxillæ of equal importance with faulty eruption of the incisor teeth in causing deviations of the septum.

Thyroid Tumor of the Tongue.—Stuart-Low (*Jour. Laryng., Rhin., and Otol.,* April, 1909) reports a case of a female patient, aged thirty-two years, with a large, firm swelling at the base of the tongue. A similar condition had existed eleven years previously, when an operation was performed. She was again operated upon for recurrence nine months ago. It was now proposed to perform a preliminary laryngotomy and split the tongue in the middle line, so as to remove the tumor radically.

Hereditary Syphilis of the Rhinopharynx.—Trapenard (*Revue hebd. de laryng., d'otol. et de rhin.,* January 30, 1909) reports two cases in children of hereditary syphilis of the rhinopharynx in which the lesions simulated lymphoid hypertrophies at the vault of the pharynx. The cases were recognized, however, and promptly cured under specific treatment.

Intranasal Rhabdomyoma.—Vail (*Laryngoscope,* December, 1908) reports this unique case in a well-nourished woman, aged fifty-eight years, who presented herself with occlusion of the left nasal passage which had gradually followed an attack of grippe six weeks previously. A growth was found completely occluding the nares and presenting post-rhinoscopically a mass of pale, light gray tissue, and feeling like a nodulated mass of tough tallow. It looked suspiciously like a sarcoma despite lack of reddish color and not bleeding when wounded. It was removed piecemeal with considerable difficulty, but without hemorrhage, and inspection seemed to show thorough removal. Microscopic inspection by Dr. Welch of Johns Hopkins University, revealed it as a case of rhabdomyoma sarcomatodes. Recurrence ensued, and an external operation for its removal revealed that it filled the antrum of Highmore completely, and that it was not adherent at its limitations. The removal of the entire mass was easily accomplished by simply lifting it out of its seat. Unfortunately, heart failure took place under the chloroform anesthesia, and in spite of the employment of every

known means of restoring cardiac power, the pulse remained small and thready, and the patient died sixty-eight hours after the operation.

Lymphosarcoma of the Frontal Sinuses.—ABERCROMBIE (*Medical Reports of the Central London Throat and Ear Hospital*, vol. i) reports a case of lymphosarcoma of the frontal sinuses in a woman, aged seventy-five years, who succumbed from erysipelas developed after a third operation for recurrence.

Chondroma of the Left Maxillary Antrum.—ABERCROMBIE (*Ibid*) reports this case in a girl, aged sixteen years. The growth was removed by operation, and in three months a second operation was required for recurrence, after which she did well. Three years after the second operation a similar though much smaller growth was removed from the antrum of the other side. Recovery was uneventful, and she left the hospital after a ten days' residence.

Apparent Primary Laryngeal Tuberculosis.—ATKINSON (*Medical Reports of the Central London Throat and Ear Hospital*, vol. i) reports a case of laryngeal tuberculosis in a man, aged sixty years, without any other manifestation. The left vocal cord presented a thickened, slightly fleshy looking appearance limited to its anterior two-thirds, with delayed sluggish movement. On the upper surface one or two enlarged vessels were observed, but nothing else in any way abnormal in any portion of the larynx. Some six weeks later, implication of the lungs became evident. Atkinson deemed this case worthy of being recorded owing to its simulating epithelioma in its early stages, and also because all the evidences, both positive and negative, point to the conclusion that it was one of primary laryngeal tuberculosis.

Subhyoid Pharyngotomy for Epithelioma of the Epiglottis.—CASTEX *Jour. Laryng., Rhin. and Otol.*, April, 1909) reports a case of a man, aged fifty-four years, from whom a growth on the epiglottis was removed by thermocautery after external access to the parts by subhyoid pharyngotomy. The after-results were very good. A second patient, however, whose case was analogous, sank rapidly thirty-six hours after the operation, with intense pulmonary oppression. Relying on this observation and on that of a laryngectomy in which the trachea had been united to the skin, Castex thinks that some of these rapid deaths are explicable by a sudden and diffuse pulmonary œdema, the cause of which perhaps is a reflex initiated in the vagus and sympathetic filaments irritated at the level of the pharynx.

Laryngotomy and Fulguration in Cancer of the Larynx.—LAURENS (*Arch. intern. de laryng., d'otol. et de rhin.*, Janvier-Fevrier, 1909) reports two cases of intrinsic carcinoma of the larynx in which direct access to the growths was secured by thyrotracheotomy, and after removal of the growth, in one case with curette and the other with scissors, electric fulguration was applied to the surface of implantation and a little beyond, for three minutes, at the end of which time the cartilages and surfaces were carbonized. Good recoveries were made in both instances, and the prospects for successful results seemed favorable.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Changes in the Arterial Blood Pressure in Heart Disease during Disturbances in Compensation.—In 1901 Sahli stated that in cases of heart disease the recovery from a break in compensation may be accompanied by a fall in blood pressure. Though the observation has been made casually several times since, there has been no systematic study of this point up to the present time. LANG and MANSWETOWA (*Deut. Arch. f. klin. Med.*, 1908, xciv, 455) have made observations upon the blood pressure in 28 cases of heart disease and 7 cases of emphysema. In 17 out of 18 cases of uncomplicated mitral disease, both the systolic and diastolic pressure fell with recovery from broken compensation. In some instances the fall in systolic pressure was as much as 30 to 40 mm., and the drop in diastolic pressure even greater. In 7 cases of emphysema there was uniformly a well-marked decrease in pressure with the onset of compensation. Only 5 of the 10 cases of aortic insufficiency and arteriosclerosis presented a fall in pressure. These results at first seem paradoxical, but if one considers the condition of the capillaries during broken compensation the explanation is evident. With the back pressure in the venous system there comes greater peripheral resistance in the capillaries, which may be at least one cause of the high pressure. Again, the cyanosis produced by the poor aëration of the blood in itself brings about a contraction of the peripheral capillaries, thus assisting in the increased pressure. It is noteworthy that in those types of heart disease in which the right side bears the brunt of the lesion and in emphysema, in which, again, the right side of the heart is principally affected, there is the most constant and marked fall in blood pressure during recovery from broken compensation. This is probably due to the fact that the left ventricle is capable of the attempt to overcome the increased peripheral resistance. In 20 of the 35 cases the pulse pressure was higher during disturbances in compensation than after compensation had been restored. No definite relationship could be determined between the appearance and disappearance of œdema and the alterations in blood pressure.

The Hematogenous Origin of Purulent Nephritis.—J. KOCH (*Zeit. f. Hyp. u. Infekt.*, 1909, lxi, Heft iii) considers the most important factor in descending purulent nephritis caused by the staphylococcus to be that staphylococci in the blood stream are excreted through the kidneys in the urine. Staphylococci, which metastasize only by the blood, are found in the blood in many local, as well as general, infections, and, as is shown by Lenhartz, are much more apt to metastasize than

streptococci (in 95 per cent. of 22 cases, while streptococci showed 35 per cent. in 160 cases). This elimination through the kidneys, however, is a pathological, not a physiological, condition; that is, some injury to the eliminating organs—a glomerulonephritis—must exist, otherwise the staphylococci in the blood stream will pass on. This injury, according to Koch, can be dealt by the toxin elaborated by the staphylococci, which are thus enabled to pass through the vessel walls of the glomeruli and the renal epithelium. Whether or not it is possible for the staphylococci secondarily to make their way through the blood-vessel walls and epithelium of the convoluted tubules is not yet determined. He distinguishes two forms of abscesses: Those arranged in groups in the cortex with streak-like prolongations into the medulla; and secondly, those in the medulla, with little or no involvement of the cortex. In experimental nephritis he finds that the former are produced by injections of virulent cultures; the latter, if the strains of staphylococci are weakened. The streak-like abscesses in the medulla arise from the tubules being blocked by casts, which then not only offer a favorable medium for the growth of the staphylococci, but allow the elaboration of toxins which damage the surrounding renal tissue and make it susceptible to extension of the abscess. Koch has found in his experiments occasional cases of chronic nephritis, perirenal inflammation, or lesions in one kidney only. He considers the demonstration of staphylococci in the urine to be of importance in the diagnosis of such staphylomycoses as pyemia, osteomyelitis, endocarditis, phlegmon, furunculosis, and carbuncles.

The So-called Abnormal Tendon Fibers of the Heart.—In 1905 TAWARA, in an exhaustive monograph on the system that conducts the contracting impulse in the heart of mammals, proved that the so-called Purkinje fibers were in reality the broadened out and modified terminations of the atrioventricular bundle of His. He later (*Beitr. zur. path. Anat.*, 1906, xxxix) asserted that the small bundles attached by one extremity to the septum of the heart and by the other to the base of a papillary muscle (the so-called "abnormal tendon fibers") are in reality nothing but Purkinje fibers which are reaching their final destination (the papillary muscles) by an abnormal route. Instead of being subendocardial, as is normally the case, Tawara claims that the fibers in these cases have become isolated from the myocardium and invested with a separate endocardial sheath. He bases his argument on the fact that the fibers arise from the interventricular septum, where the left branch of the bundle of His terminates, and end in a papillary muscle, where the Purkinje fibers also terminate. MÖNCKEBERG, however, takes exception to this claim (*Verhandl. d. deut. path. Gesell.*, 1908, S. 160), and proves that in many cases, at least, the bundle of His or the Purkinje fibers are not contained in these fibers. By studying them microscopically and in serial sections at their origin and insertion, he was able to demonstrate four distinct types: one in which there were no muscular elements of any kind; a second consisting of normal heart muscle (*i. e.*, a connecting bridge between septum and papillary muscle); a third consisting wholly of a continuation of the left branch of the bundle of His (*i. e.*, the same as those described by Tawara); and a fourth made up of both normal heart muscle and the continuation of the left branch (*i. e.*, combination of second and third).

In this connection it is interesting to note the observations of SAIGO (*Verhandl. de deut. path. Gesell.*, 1908, S. 165) on the part played by Purkinje fibers in diseases of the myocardium. In such regressive changes of the myocardium as fatty degeneration, necrosis, connective tissue increase, etc., he finds that these fibers are always more or less involved. The perivascular nodules found in the myocardium by Aschoff and Geibel in cases of acute rheumatic fever were also found to invade the Purkinje fibers. In brown atrophy or hypertrophy of the heart, however, the Purkinje fibers were found to be distinctly less involved than the rest of the heart muscle.

In the same journal (p. 150) there is a short communication by ASCHOFF, with two illustrations showing the presence of glycogen in the Purkinje fibers. This, in connection with the morphology of the impulse-conducting system (that is, narrow, incompletely striated fibers, with numerous nuclei) is taken as another proof of their intermediate position between adult and embryonal heart muscle.

The Disappearance of Trypsin in the Circulation.—Since von Bergmann and Guleke have shown that with the destruction of a large portion of the pancreas in the body, substances are formed which when absorbed lead to fatal intoxication, it seemed possible to BAMBERG (*Ztschr. f. exp. Path. und Therap.*, 1909, xv, 743) that in less marked disturbances of the pancreas trypsin might be absorbed and ultimately eliminated by the kidneys in the urine. This led him to repeat some of the experiments upon the appearance of trypsin in the urine under normal and pathological conditions. By a method which enabled Bamberg to detect a quantity of trypsin equal to 5 decimilligrams of the dried trypsin powder he was unable to obtain tryptic digestion in the urine from fourteen normal men and eight dogs. Injection of trypsin into dogs demonstrated that only after very large amounts had been given could trypsin be found in the urine. Transplantation of the pancreas of one dog into the abdomen of another led to extensive fat necrosis, toxemia, and death, but only once in six experiments was trypsin eliminated in the urine. After considering the various possibilities which might account for the disappearance of the trypsin in the body, Bamberg finally concludes that it is in some way made ineffective by the antitryptic property of the blood serum. In none of his experiments was the antitryptic property of the blood serum overneutralized. The blood serum in no instance showed tryptic properties, but rather an increase over the normal of antitryptic property.

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